

# THE American Journal OF Gastroenterology

VOL. 24, NO. 5

NOVEMBER, 1955

Unusual Problems in Biliary Tract Surgery

Medical Aspects of Noncalculous Gallbladder Disease

Surgical Approach to the Problems of Gallbladder Disease

Gastrointestinal Hemorrhage:

Therapeutic Evaluation of Bio-Flavonoids

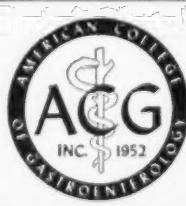
A New Approach to the Management of Peptic Ulcer  
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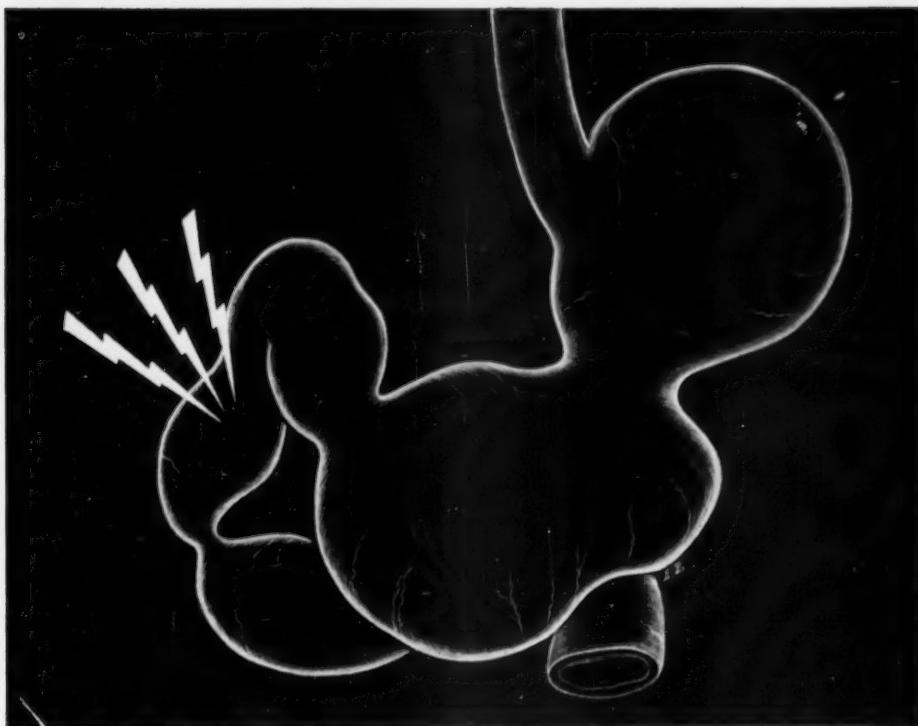
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2. Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., Jr., and Texler, E. C., Jr.: Mechanism of Pain in Peptic Ulcer, *Gastroenterology* 23:252 (Feb.) 1953.

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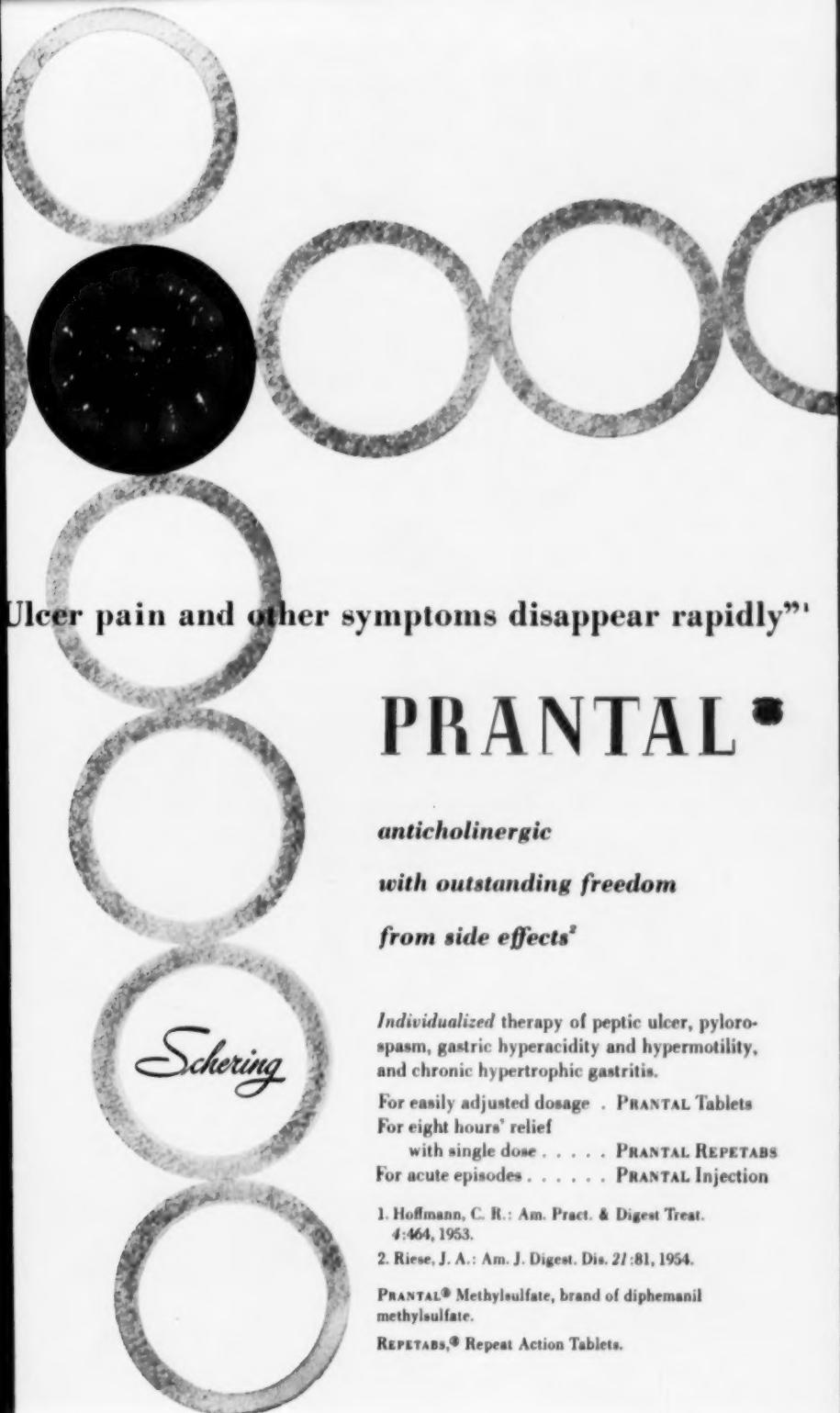
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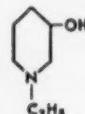
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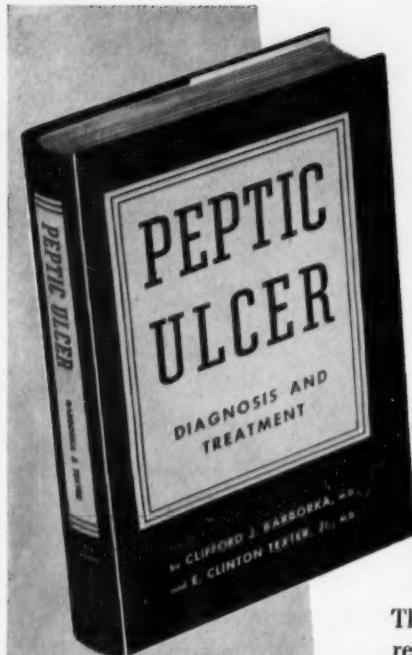
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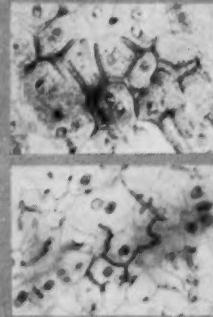
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## UNUSUAL PROBLEMS IN BILIARY TRACT SURGERY\*

ROBERT J. COFFEY, M.D.†

and

NIZAR OWEIDA, M.D.‡

Washington D.C.

This subject will, I am sure, provoke misgivings in the minds of many who have had extensive experience in this field of surgery. This stems from the fact that unusual problems are actually commonplace in biliary tract surgery. The intimate anatomic and functional relationship of the gallbladder and extrahepatic biliary ducts with the stomach, duodenum and pancreas makes for frequent association of pathologic conditions of these organs. Furthermore, the inexactness of preoperative demonstration of the pathology to be anticipated is in striking contrast to lesions of the stomach or colon where one can in a great majority of cases clearly demonstrate by roentgenologic methods the lesion.

Since we have repeatedly encountered unique problems in the field of biliary tract surgery, we have reviewed our available records of the past five years for such cases. It soon became evident that these unusual problems fell into two large groups, namely, those in which biliary tract disease was associated with other visceral lesions, and, secondly, those cases in which unusual pathologic or anatomic findings were encountered at the time of surgery.

### ASSOCIATED BILIARY TRACT DISEASE

1. *With Cardiac Disease:*—Since it is not within the scope of this discussion to consider this subject comprehensively, it suffices to state that the problem concerns, on the one hand, those cases in which symptoms arising from biliary

\*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Washington, D.C., 28, 29, 30 October 1954.

†Professor of Surgery and Director of Department of Surgery.

‡Senior Assistant Resident in Surgery, Georgetown University Medical Center, Washington, D.C.

tract disease have been mistakenly attributed to cardiac disease, and, on the other hand, those cases in which both biliary tract disease and cardiac pathology coexist. In this series several noteworthy problems that are deserving of mention were encountered.

a. *Cardiac Arrhythmia*:—Surgical correction of coexistent biliary tract disease, namely, chronic cholecystitis with stones, may be indicated in the case of cardiac arrhythmia with or without demonstrable organic heart disease. In the following case the potential danger of surgical anesthesia as well as the desirability of continuous electrocardiographic recording during the course of such an operation was clearly demonstrated.

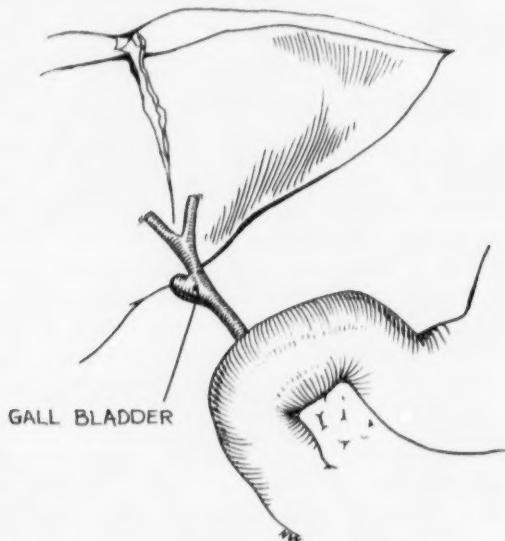


Fig. 1—Hypoplasia of the gallbladder.

*Case 46024*:—E.W., a white female, age 44, was admitted for cholecystectomy. She had complained of cardiac palpitation for two years. Frequent extrasystoles, demonstrated by electrocardiography, were controlled by quinidine. No other evidence of organic heart disease was observed. Recurrent bouts of right upper abdominal pain and fatty food intolerance of ten months' duration led to the cholecystographic visualization of gallstones.

On induction of anesthesia with a pentothal-nitrous oxide-oxygen combination, a continuous electrocardiographic recording revealed gradual widening of the P-R interval, eventuating in heart block. This occurred in association with a moderate fall in blood pressure. Anesthesia was discontinued with a prompt return of atrioventricular association.

Although the projected cholecystectomy may have been carried out without serious incident, continuation of the operation in the presence of heart block would have been imprudent. Cholecystectomy is planned later, at which time the consulting cardiologist has recommended liberal atropine therapy.

b. *Associated Paroxysmal Dyspnea*:—Paroxysmal dyspnea developing in the patient with coronary heart disease may be interpreted as a contraindication to the eradication of coexisting biliary tract disease. In the following case, however, removal of the diseased gallbladder was followed by decided improvement in the paroxysmal dyspnea.

*Case 31569*:—P.McA., a white male, age 51 years, complained on admission of epigastric pain, paroxysmal dyspnea, and orthopnea of two weeks' duration. A similar episode was experienced two years previously. Electrocardiographic evidence of myocardial infarction had been repeatedly demonstrated. A cholecystogram revealed a nonfunctioning gallbladder with stones.



Fig. 2—Stenosis of the cystic duct proximal to which a very small stone was impacted.

Under general anesthesia a markedly thickened gallbladder containing multiple stones, one of which was impacted at the cystic duct, was removed. His postoperative course was marked by a brief episode of pulmonary edema. The paroxysmal dyspnea was remarkably improved.

Following discharge he returned to active business life. Eighteen months later, however, he was readmitted with recurring symptoms of coronary insufficiency.

c. *Acute Pulmonary Edema During Surgery*:—In four instances in which gallbladder surgery was carried out in the presence of demonstrable heart disease, the operation was complicated during its course or immediately thereafter by the development of acute pulmonary edema. In three of these a history of congestive heart failure was lacking. Fortunately, the prompt identification of this complication permitted early and energetic institution of treatment with survival of each patient.

*Case 17743:*—D.F., a white female, age 46 years, developed severe right upper abdominal pain with nausea and vomiting two weeks before admission. Although a known case of hypertensive heart disease of five years duration, there had been no recent symptoms of cardiac decompensation. Blood pressure 240/120 mm. Hg. Cholecystogram revealed a poorly functioning gallbladder containing multiple stones.

Cholecystectomy was carried out on the fifth hospital day. On the completion of the operation hypotension developed in association with severe acute pulmonary edema. Artificial respiration was required. Intravenous aminophylline and cedilanid were administered. Approximately 300 c.c. of frothy fluid was recovered from endobronchial aspiration. After two hours the blood pressure became stabilized at 180/110 mm. Hg., the cyanosis disappeared, and she regained consciousness.

The development of acute pulmonary edema during operations on cardiac cases should be anticipated. Preoperative digitalization is recommended in



Fig. 3—Traumatic rupture of the gallbladder.

those cases with a history of congestive failure, and of course in those with existing evidence of failure, full compensation should, if possible, be established before surgery. Emergency measures, including application of tourniquets to the extremities, endobronchial aspiration, intravenous aminophylline and cedilanid may be life-saving in the treatment of this complication.

2. *With Pancreatic Disease:*—The association of either acute or acute recurrent pancreatitis with biliary tract disease has been repeatedly emphasized. In a review of 184 cases of acute pancreatitis by one of us (RJC) this relationship was demonstrated in 18 per cent of the cases, in two-thirds of which the cholecytic disease was of the chronic calculous type while in one-third acute cholecystitis was present<sup>1</sup>. The diagnosis of pancreatitis in these cases rests upon the demonstration of an elevated serum amylase level although the clinical symptoms may point clearly to the presence of biliary tract disease.

In cases with associated acute cholecystitis and acute pancreatitis conservative treatment should be instituted. In three of the eleven cases in this series, however, threatened or actual perforation of the gallbladder necessitated emergency surgical intervention.

In cases with associated chronic cholecystitis and acute pancreatitis conservative measures are employed. On subsidence of the acute pancreatitis, however, cholecystectomy undoubtedly exerts a favorable influence on the pancreatic pathology.

It should be pointed out that demonstration of the associated cholecystitis by cholecystography is most undependable during the early weeks following the subsidence of the acute pancreatic attack.

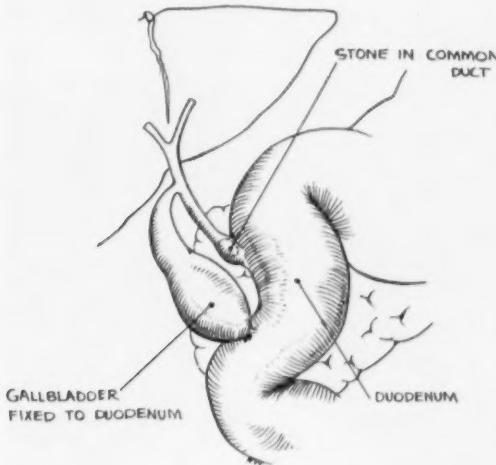


Fig. 4—Cholecystoduodenal fistula with a common duct stone.

3. *With Hemolytic Anemia*:—The association of a calculous gallbladder disease with hemolytic anemia is well known<sup>2</sup>, resulting from the abnormal hemolysis of blood with an unusual concentration of bile pigments in the biliary tract. In nine cases of hemolytic anemia in which splenectomy was carried out, calculous disease of the gallbladder was demonstrated in five. In each instance it was possible by means of extension of the splenectomy incision to remove the calculous gallbladder as a one-stage procedure.

A particular problem arising in this relationship concerns the error of attributing jaundice resulting from a common duct stone to a hemolytic crisis.

*Case 71077*:—T.S., a white male, age 27 years, was admitted with an eight week history of recurring right upper abdominal colic and jaundice. Acholic

stools and dark urine had been noted. At the time of a previous hospitalization five years ago because of jaundice and splenomegaly a diagnosis of congenital hemolytic anemia was made.

A hematologic survey established the diagnosis of congenital spherocytic icterus—icterus index 50. Cephalin flocculation test—2 plus in 48 hours. The spleen extended 5 cm. below the costal margin.

Splenectomy was carried through a transverse incision. Numerous stones were palpated in the gallbladder. An enlarged common bile duct was opened and explored. Two medium sized common duct stones were removed. Convalescence was uneventful.

The acholic stools in association with typical gallstone colic suggested the obstructive nature of the jaundice in this case. Consequently, the common duct was carefully inspected and explored.



Fig. 5—Round-worm extruded through a T-tube.

4. *With Esophageal Hiatus Hernia*:—In this series four cases of associated biliary tract disease and esophageal hiatus hernia were encountered. In view of the fact that the symptomatology resulting from either of these lesions may closely simulate the other, it is often difficult to determine the role that each lesion plays in the production of symptoms. In one case cholecystectomy was followed in the early postoperative period by the recurrence of the pre-operative complaints, and it was only after repair of the hiatus hernia that the symptoms were eliminated. In two cases the hiatus hernia was of such small size that it was correctly interpreted as being inconsequential. It may, however, be necessary on occasion to correct both conditions simultaneously.

*Case 12032*:—M.D., a white female, age 61 years, was admitted with the complaints of mild right upper abdominal pain, epigastric fullness and belch-

ing for two years. She had lost 12 pounds in six months. For ten years she had periodically been awakened at night with "a mouthful of grease". A cholecystogram revealed multiple calculi. An upper gastrointestinal x-ray study demonstrated the presence of a large esophageal hiatus hernia, containing one-third of the stomach.

At operation a chronically diseased gallbladder with stones was removed. A large esophageal hiatus defect, admitting a fist, was repaired with interrupted silk sutures. Convalescence was uneventful.



Fig. 6—Flat plate showed calcification of gallbladder and a calcific shadow that proved to be due to calcification of the wall of the common duct.

5. *With Duodenal Ulcer:*—The demonstration of a duodenal ulcer in the patient with calculous disease of the gallbladder poses an extremely perplexing problem. Although in some cases the symptomatology is characteristic of one or the other lesion, an assessment of the role of each must be made at times by the operating surgeon.

*Case 37180:*—G.C., a white male, age 59 years, was known to have a duodenal ulcer for twenty years. One attack of hematemesis occurred two years

previously. Three weeks prior to admission he developed severe epigastric pain which radiated to the region of the right scapula. The gallbladder failed to visualize on cholecystography.

On surgical exploration a subacutely inflamed gallbladder without stones was found and removed. A badly scarred duodenum with evidence of an active duodenal ulcer was encountered. A vagotomy and posterior gastrojejunostomy was carried out. He has been asymptomatic since then.

#### UNUSUAL ANATOMIC AND PATHOLOGIC FINDINGS

At the time of surgical exploration of the biliary tree many perplexing findings may confront the surgeon. In the interest of classification these will be considered according to their anatomic site.

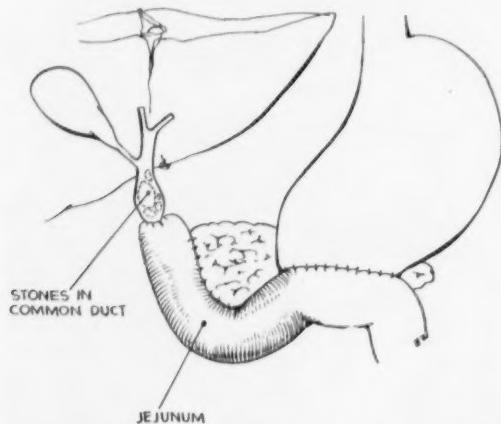


Fig. 7—Common duct stones proximal to choledochojejunostomy.

1. *Gallbladder*:—a. *Agenesis of the Gallbladder*:—Congenital absence of the gallbladder more often than not occurs as a part of complete agenesis of the extrahepatic biliary tract. In most cases operative cholangiography should be carried out in order to eliminate the presence of an intrahepatic gallbladder. In one case in which this anomaly was encountered, the cholangiogram revealed absence of the gallbladder.

b. *Hypoplasia of the Gallbladder*:—In two instances a rudimentary gallbladder, constituting no more than an outpouching of the common bile duct, was found. In both cases the presence of common duct stones and the marked thickness of the wall of the rudimentary organ pointed to an inflammatory basis for this condition (Fig. 1).

c. *Stenosis of the Cystic Duct*:—Although stenosis of the cystic duct has not been stressed as a significant finding, the following case suggests its probable role in the production of gallbladder symptoms.

*Case 54678*:—G.T., a white female, was admitted for cholecystectomy. For seven years she had experienced typical attacks of biliary colic without jaundice. Fatty food intolerance was conspicuous. On cholangiography the gallbladder failed to visualize.

At operation a thin-walled, apparently normal gallbladder without palpable stones was found. A minute cystic duct was identified. Several enlarged, greenish-black lymph nodes along a normal common duct were observed.

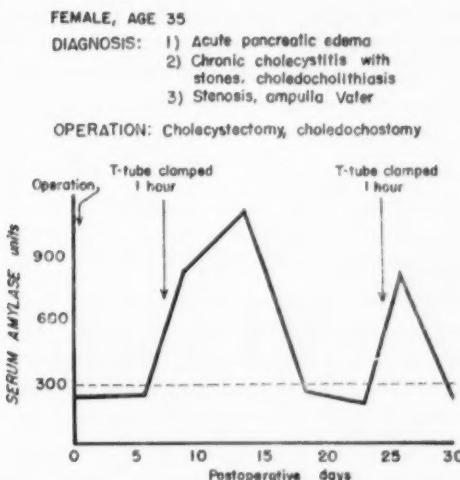


Fig. 8—Recurring serum amylase elevation and stenosis of ampulla of Vater. (Coffey, Robert J.: The Relationship of Acute and Chronic Cholecystitis to Acute Pancreatitis. Southern M. J. 47:448-451, 1954.)

After removal of the gallbladder, it was found to contain several very small calculi whose size obviously precluded their passage through the tiny cystic duct (Fig. 2). An excised lymph node showed on histopathologic study reactive changes with conspicuous deposition of bile pigment throughout its structure.

d. *Traumatic Rupture of the Gallbladder*:—Nonpenetrating trauma of the abdominal wall infrequently results in gallbladder injury. When it does occur, avulsion of the gallbladder from the liver bed may result or, as occurred in one of our cases, actual rupture with bile peritonitis may take place (Fig. 3).

e. *Cholecystenteric Fistula*:—Although fistulization between the gallbladder and the intestinal tract results in gallstone ileus in only 10 per cent of cases, the

calculi within the gallbladder are usually extruded into the bowel. While a cholecystocolonic fistula should be eliminated by means of cholecystectomy, the more common cholecystoduodenal fistula in most cases does not require surgical correction<sup>3</sup>. In one such case, however, surgical intervention was clearly indicated.

*Case 18684*—N.C., a white female, age 53, was admitted with clinical evidence of low intestinal obstruction. On surgical exploration an obstructing gallstone was found in the terminal ileum, and removed. Dense adhesions between the gallbladder and duodenum were palpated.

Twenty months later she was readmitted because of jaundice, acholic stools, anorexia and a 20 pound weight loss over a two month period. Laboratory studies indicated the presence of an obstructive jaundice. At the time of surgical exploration four large stones were removed from the dilated com-

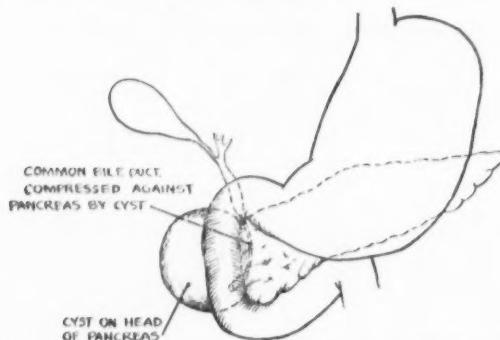


Fig. 9—Obstructive jaundice due to pseudocyst of pancreas. (Coffey, Robert J.: Unusual Features of Acute Pancreatic Disease. Ann. Surg. 135:715-720, 1952).

mon duct. On removal of the gallbladder, intimate fixation to the duodenum was found, but no actual fistulous communication could be demonstrated (Fig. 4).

Postoperative convalescence was uncomplicated.

2. *Common Duct*—The presence of obstructive jaundice, a common indication for surgical exploration of the biliary tract, leads the surgeon into many and varied problems. Probably in no other field of surgery must the operator be more prepared for unsuspected findings.

a. *Ascariasis of the Common Duct*—Although invasion of the common duct by round worms is reported as being not uncommon in endemic areas, its occurrence in this area is most unusual.

*Case 47862*—White female, age 3 years, was admitted for antihelminthic therapy because of the passage of round worms per rectum. Repeated courses

of treatment failed to eliminate ova from the stools. Irregular fever and hepatomegaly developed. Several acholic stools were observed but no jaundice occurred. The gallbladder did not visualize on cholecystography.

On the basis of a preoperative diagnosis of ascaris infestation of the biliary tree, surgical exploration was carried out. In addition to removal of several round worms from the common duct, round worms were evacuated from three chronic abscesses of the liver. T-tube drainage of the common duct was established.

On the third postoperative day a round worm extruded itself along the T-tube (Fig. 5). After a slow recovery, her stools finally became ova-free three months later.

b. *Calcification of the Common Duct*:—Although calcification of the gallbladder wall, apparent on x-ray of the abdomen, is not uncommon, similar, ring-like calcification of the wall of the common duct is most unusual. In one of our cases this calcification of the wall of the common duct was evidently responsible for the existing jaundice (Fig. 6).

c. *Rupture of the Common Duct in the Newborn*:—The following case, unique in our experience, probably represents a congenital abnormality of the common duct related to the development of a choledochal cyst.

*Case 6916*:—L.F., a white male, age 22 days, was noticeably jaundiced at birth. The stools were acholic. After excluding congenital syphilis and erythroblastosis foetalis, a diagnosis of congenital atresia of the bile ducts was considered. After 17 days the jaundice lessened and simultaneously evidence of ascites was observed. On needle aspiration through the abdominal wall, deeply bile-stained fluid was recovered.

Surgical exploration was carried out on the 21st day. After aspiration of a large amount of bile-stained fluid, a defect in the common duct wall was identified, from which free leakage of bile was taking place. An anastomosis between this aperture and the jejunum was established. The infant recovered without incident.

Three months after discharge he suddenly expired at home. An autopsy was not obtained.

d. *Residual Common Duct Stones*:—It has been stated that it is the inexperienced operator who has never committed the surgical error of overlooking stones in the common duct. Although this error has not been unusual in our experience, in one exceptional case an impacted common duct stone was found following a Whipple pancreaticoduodenectomy for carcinoma of the ampulla of Vater (Fig. 7).

3. *Ampullary Lesions*:—a. *Stenosis at the Ampulla of Vater*:—Stenosis at the ampulla of Vater can, in the occasional case, be demonstrated at the time

of surgery. That such a lesion does occur and that it permits reflux of bile into the pancreas has been clearly demonstrated in several of our cases. Clamping of the T-tube in such cases may be promptly associated with the development of upper abdominal pain and an elevation of the serum amylase (Fig. 8).

b. *Chronically Impacted Stone at the Ampulla:*—Much has been said about the so-called "silent common duct stone". The presence of such a stone for a long period of time without jaundice may occur, and pose a difficult diagnostic problem. In one case the basis for recurring chills and fever was obscure for 16 months at which time jaundice appeared. Likewise a chronically impacted stone at the ampulla with an unusual degree of attendant inflammation may present a clinical picture strongly suggestive of carcinoma of the head of the pancreas. In one such case a radical pancreaticoduodenectomy was narrowly averted.

c. *Pancreatic Pseudocyst Causing Common Duct Obstruction:*—An uncommon cause of obstruction of the lower end of the common duct is the development of a peripancreatic collection arising from the head of the pancreas after pancreatitis. Evacuation and drainage of such a cyst in two cases resulted in prompt disappearance of the jaundice (Fig. 9).

d. *Chronic Pancreatitis with Common Duct Obstruction:*—Chronic pancreatitis with common duct obstruction may mimic carcinoma of the head of the pancreas. A radical pancreaticoduodenectomy was carried out in the case of an elderly male with painless and progressive jaundice, marked weight loss, and a palpably enlarged gallbladder. The mass palpated in the head of the pancreas at the time of surgical intervention proved to be a chronically inflamed gland.

#### SUMMARY

From a large series of cases of biliary tract disease a group illustrating unusual problems were selected. These cases were categorized into those in which biliary tract disease was associated with other significant conditions, and those in which unusual anatomic or pathologic findings were encountered.

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#### DISCUSSION

*Dr. I. Snapper:*—The cause of accidents in surgery is often human negligence. Therefore, there are probably no more accidents in very old people or cardiac

patients operated upon than in young noncardiac patients because extra care is taken during the operation of a cardiac patient.

Pulmonary edema is a good example. It is due to overloading of the small circulation and occurs when too much circulating blood volume is present in a patient with a damaged left heart. Restriction of the amount of saline or blood given after operation will help prevent postoperative pulmonary edema in cardiac patients.

Cardiac arrhythmia during operation may be caused by the struggle which occasionally occurs when the tracheal tube is inserted. Many people can be intubated easily, but some people cannot. In such cases the arrhythmia can be prevented by giving a whiff of ethyl chloride, or ether during the intubation.

Ascariasis of the biliary ducts is known to be a very dangerous complication. This is also evident in Dr. Coffey's case where liver abscesses had developed.

*Dr. O. H. Wangensteen:*—Dr. Coffey covered the whole range of the problems of biliary tract surgery in an interesting way. I will add to what Dr. Snapper said concerning anesthetic difficulties, that introduction of a dilute cocaine solution through the thyroid cartilage into the trachea, can obviate the sort of anesthetic difficulty of which Dr. Coffey spoke.

I shall make only one additional comment, and I do so in the light of circumstances that I know that many of you have the opportunity of seeing many more patients with acute biliary tract disease than I. There is still today a moot question of whether one should do emergency operations for acute cholecystitis or whether it is preferable to delay. I have had the opportunity in a few instances to measure the pressure in the acutely obstructed gallbladder at operation, and I have found the intraluminal pressure in a few instances to be as high as 40 cm. of saline solution. That is not a high physiologic pressure, but it is higher than capillary blood pressure, and when that happens in any viscus, whether in the intestine or in an appendage thereto, it will lead to a deleterious and serious threat to the viability of the wall of the viscus concerned. The absence of a bacterial flora in the normal gallbladder makes the situation less hazardous than in the intestine, and consequently the ill effects from an obstruction of the biliary bladder is not so great. In the intestine, however, an intraluminal pressure of 20 cm. of saline solution, continuing over a period of 24 hours or more, leads to nonviability of the gut wall. If this observation of an elevated intraluminal pressure within the obstructed gallbladder is duplicated in the experience of many of you, you can readily understand how one could justify on good grounds a more deliberate surgical attack upon the acutely obstructed case.

I would commend to any of you who, during the course of the next year, have the opportunity to operate on a patient with acute cholecystitis to do it early and to measure the intraluminal pressure. We need more evidence of

this sort. The establishment of what the intraluminal pressure is within the gallbladder in a series of cases of acute cholecystitis can help resolve what the best therapy is. It can be said that sustained pressures exceeding capillary blood pressure (30 mm. saline solution) are distinctly hazardous for the survival of any organ, whether its lumen normally contains bacteria or not. I have seen a few instances in which the pressure within the obstructed gallbladder was only 10 cm. of saline solution, but there have been others in which the pressure was in the range of 30 to 40 cm. of saline solution, which shows pretty definitely that more obstructed gallbladders should be operated upon early. Moreover, we know that in the small bowel a continued intra-luminal pressure of 10 to 14 cm. of saline solution—a pressure less than the upper range of portal venous pressure (16-20 cm. saline solution) will wreck havoc upon the gut wall if continued for more than 24 hours. The same is probably true of the gallbladder, though the process may be less rapid because of the difference in bacterial flora.

## MEDICAL ASPECTS OF NONCALCULOUS GALLBLADDER DISEASE\*

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I should like to preface my remarks by confessing that I have always looked at noncalculous cholecystitis with, to use what may perhaps be an apt phrase, a "jaundiced" eye. Minor morphologic changes admittedly are commonly found in stoneless gallbladders removed at operation or examined at autopsy. That these changes are responsible for clinical symptoms, however, is dubious at best. This is not meant to infer that clinically significant noncalculous cholecystitis does not occur. I have seen sufficient shrunken, fibrotic, and even calcified gallbladders ever to doubt the existence of such a disorder.

### DIAGNOSIS

It is my thesis that the diagnosis of chronic noncalculous cholecystitis is one that is made much too often on unconvincing evidence. Diagnosis of a disorder of this type should be supported by objective findings and not be based on subjective symptoms alone.

For an acceptable diagnosis of noncalculous cholecystitis, the clinical expressions should be strongly suggestive of those for which disease of the gallbladder is commonly responsible. The most important symptom in this regard is biliary colic. In the absence of classical biliary colic, there may be complaints of lesser degrees of pain and discomfort in the region of the gallbladder. These complaints are all the more suggestive of gallbladder disease if they tend to occur after eating a heavy and fatty meal, or after jarring or jolting.

Another type of symptom-complex that may be seen in patients with noncalculous disease of the gallbladder is one that mimics peptic ulcer disease. This form of distress is related to the eating of meals and is especially likely to occur after heavy or fatty meals. It may occur only after some meals and not others. It is frequently epigastric in location. Relief may be obtained by assuming certain postures, a feature not common to peptic ulcer. It differs from ulcer, also, in its irregular and brief occurrences and in its lack of periodicity. This symptom-complex, referred to by Bockus<sup>1</sup> as the pyloroduodenal syndrome, is thought to be due to pericholecystitis with adhesion formation about the pyloroduodenal segment.

\*Read as part of the Panel Discussion on "Twenty-five Years' Observation of the Gallbladder Controversy", before the First Annual Convention of the American College of Gastroenterology, Washington, D. C., 25, 26, 27 October 1954.

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Other dyspeptic symptoms, such as belching, bloating, flatulence, and so-called qualitative dyspepsia are often due to causes other than chronic cholecystitis. This is true even in the case of the stone-bearing gallbladder. It cannot be denied that such symptoms may be improved by removing a diseased gallbladder. When this occurs, it would seem reasonable to suppose that these symptoms were related in some way to the diseased gallbladder. Nevertheless, one cannot offer assurance in a given patient that such symptoms, if present, will be relieved by cholecystectomy. It must be remembered that even patients with gallstones are subject to other disturbances capable of producing similar symptoms. Among these may be mentioned improper mastication, hiatus hernia, irritable colon, and emotional disorders causing functional derangement of various segments of the gastrointestinal tract.

Objective evidence to support a clinical impression of noncalculous cholecystitis is most often provided by roentgen examination of the gallbladder. Properly performed cholecystography, however, demands the use of every available maneuver in order to be certain that stones are not present. Such maneuvers include a roentgenogram made with the patient in the erect position. The value of this examination is illustrated in the subject whose cholecystograms are shown on this slide (Slide). Roentgenograms obtained when the patient was supine failed to show calculi; the film taken with the patient erect, however, clearly shows layering of multiple radiolucent stones.

It is important, too, to repeat the cholecystographic study if the symptoms strongly suggest calculous disease but previous roentgenographic examination has been nonrevealing. This is illustrated by the slides of the next subject in whom two previous cholecystographic studies were reported as negative. On the third examination, however, multiple radiolucent calculi were successfully demonstrated (Slide).

Gallstones in the ducts, which might escape detection by orthodox oral cholecystography, may be visualized when contrast medium is given intravenously. The next slide illustrates the usefulness of intravenous cholecystography and cholangiography (Slide). Multiple calculi are demonstrated in the gallbladder and in the common duct as well. The latter are clearly shown in the roentgenograms exposed before as well as after the gallbladder became visible.

Slight diminution in the degree of opacification of the gallbladder after orally administered contrast media is not sufficient evidence on which to base a diagnosis of noncalculous cholecystitis; nor is failure of the gallbladder to contract or empty after the ingestion of fat or fatty substances. One should insist that the concentrating power of the gallbladder be shown to be significantly impaired. This requires persistent nonvisualization, or markedly diminished opacification, demonstrated on repeat examination using a double dose of the oral medium. In such instances, it would seem wise to follow through

with intravenous cholecystography. It has been our experience that in some such cases, the gallbladder will visualize when the contrast medium is given intravenously.

Roentgen examination of the upper gastrointestinal tract may provide evidence to support a diagnosis of chronic cholecystitis in some patients whose gallbladders visualize and do not contain calculi. This is true particularly for those with the so-called pyloroduodenal syndrome. Barium meal study of such patients may demonstrate deformity of the pyloroduodenal segment with fixed attachment of the gallbladder, the result of pericholecystitis.

Duodenal biliary drainage is another diagnostic approach of great usefulness. This examination will help exclude the presence of calculi. The existence of the latter is evidenced by the presence of cholesterol crystals and calcium bilirubinate pigment (Slide). When cholesterol crystals alone are found, stone or cholesterosis may be suspected.

Another helpful finding on bile drainage is the presence of giardia. In some instances, the symptoms suspected of being due to noncalculous cholecystitis may disappear after appropriate treatment for the giardiasis.

Evaluation of other findings on microscopic examination of sediment of the duodenal aspirate is difficult. There is an unfortunate temptation to attach more significance to these findings than they often deserve. The presence of bacterial colonies (Slide), mucus (Slide), or rows of exfoliated, bile-stained epithelial cells (Slide) are alone insufficient evidence on which to base a clear-cut diagnosis of disease of the gallbladder. An excessive amount (and I hope I shall not be asked to define "excessive amount") of such material in the concentrated fraction of bile would certainly suggest some inflammatory or catarrhal biliary process. It must be considered, however, that similar findings could also result from irritation or inflammation of the duodenum. They deserve to be given more credence as evidence of gallbladder or biliary tract disease when they are found in a patient whose gallbladder shows impaired concentrating ability on cholecystography.

Still another diagnostic approach is through the use of tests that measure the reservoir function of the gallbladder. Agents that stimulate the flow of bile are given. The ability of the gallbladder to store bile is then assayed by measuring the volume and the biliary pigment content of material aspirated from the duodenum. Gastric and duodenal contents are separately collected through a double-lumened tube or two separate tubes. After a basal period during which fasting contents are aspirated, secretin is given intravenously and aspirations continued for up to 80 minutes thereafter. The icterus index of the material obtained from the duodenum is then determined and the values plotted to construct a curve (Slide). The theory, briefly, is this: Bile is usually present to some degree in the fasting duodenal contents; the out-pouring of pancreatic juice after secretin dilutes the bile normally present and lessens the intensity

of the yellow color of the duodenal contents; at the same time the increased flow of bile, also stimulated by secretin, is stored in the gallbladder, thereby diminishing still further the biliary pigment content in the duodenum; as the flow of pancreatic juice diminishes and the distended gallbladder contracts, the bile content of the duodenal contents progressively increases until the situation that existed prior to administration of secretin is once again restored. When the gallbladder has been removed, or when its reservoir capacity is reduced by disease, the degree of yellowing of the duodenal contents is greater than normal. This is depicted by a higher icterus index level in the fasting state and a more sustained icterus index curve after secretin than is seen in normal subjects.

Sodium dehydrocholate (10 c.c. of 20 per cent solution) may be given instead of secretin. This hydrocholeretic drug causes an even greater flow of bile than does secretin and imposes a heavier load on the expansile capacity of the gallbladder. Further, it does not influence pancreatic secretion. In subjects with normally functioning gallbladders, the duodenal volume and icterus index curve both fall after the intravenous administration of sodium dehydrocholate. Patients with gallbladders that are incapable of normal distention and storage show an increase in volume; the icterus index curve is said by some<sup>2</sup> to fall and by others<sup>3</sup> to rise.

#### TREATMENT

Patients with acceptable evidence of noncalculous cholecystitis are managed in the same way as those with calculous disease of the gallbladder. In both groups, cholecystectomy is the procedure of choice. If operation is contraindicated by reason of age or attendant systemic condition, resort must be had to medical management. This, too, should not be different from that employed for patients with cholelithiasis. Such management includes the use of a low fat diet and other measures designed to diminish gallbladder activity.

There is a group of equivocal cases in which one is not sure if the gallbladder is really diseased. In these borderline cases, attempts are commonly made to stimulate rather than depress gallbladder activity. Such efforts are predicated on the hypothesis that biliary stasis may be a factor and that stimulation of biliary activity may counteract this state and discourage the formation of stones or infection. The regimen employed consists of a high fat diet, conjugated unoxidized bile salts to aid digestion, and hydrocholeretic, unconjugated, oxidized bile acids to provide active flushing of the biliary ducts. An emulsifying agent, such as Tween 80 may also be used. Antibiotics may perhaps be justified if a pure culture of organisms was obtained from the duodenum on diagnostic bile drainage. So-called therapeutic nonsurgical or duodenal biliary drainage, in my opinion, has no place in the treatment of this or related disorders.

Clinical improvement on a regimen of the type just described does not constitute conclusive proof that the condition treated was that of noncalculous cholecystitis. It should not be forgotten that we are dealing with unproved disease and that we are employing theoretical management. Above all, therapy of this type in borderline cases of this nature should not be mistakenly accepted as the treatment of choice for patients with convincing evidence of noncalculous cholecystitis.

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## SURGICAL APPROACH TO THE PROBLEMS OF GALLBLADDER DISEASE\*

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It is certainly in order that a surgeon should follow two medical men on this particular subject because what I have to say about noncalculous gallbladder as an entity would be so insignificant that it would not be worthwhile talking about it. The condition is an entity to the medical man, but, as this discussion goes on, I am going to talk about some exceptional cases.

I would rather call this, "Biliary Tract Surgery with Particular Reference to the Noncalculous Gallbladder", instead of "Surgery of the Noncalculous Gallbladder". I agree with Dr. Sexton that there are noncalculous gallbladders with symptoms, and to my mind, they are due to biliary tract disease.

As to those cases due to biliary tract disease the relief of symptoms and restoration of health can be assured to the great majority of patients to whom surgery is truly indicated.

An accurate diagnosis is essential in the treatment of biliary tract disease, and as you have heard, many organic or functional disturbances may produce symptoms simulating those characteristic of this condition.

Much information can be learned from the history of the patient. I think both of the previous speakers have brought this point out. A true, well-taken history and a complete physical examination must be done as a means of establishing a correct diagnosis. Laboratory procedures and x-ray examination may be very helpful in establishing the diagnosis.

Biliary disease may be asymptomatic at times but co-exist with other abnormalities producing similar symptoms. Knowledge and experience in this field of surgery is the surgeon's greatest asset. The problems that confront the surgical man when considering the association of gallstones or biliary disease and heart disease are many, but the three most important ones, according to Patterson<sup>1</sup> are: 1. "Mimicry" which makes differential diagnosis extremely difficult. 2. "Co-existence" which requires accurate assessment of the role of each condition. 3. "Decision" whether gallstones or biliary disease may aggravate coronary disease. Differentiation between the two conditions is extremely important for a patient with coronary heart disease might be subjected unnecessarily to a laparotomy or a needed cholecystectomy might not

\*Read as part of the Panel Discussion on "Twenty-five Years' Observation of the Gall-bladder Controversy", before the First Annual Convention of the American College of Gastroenterology, Washington, D. C., 25, 26, 27 October 1954.

be done on a patient with gallstones because the symptoms appear to be those of coronary heart disease.

Biliary tract pain is often substernal rather than abdominal. It takes a course along the 7th and 8th thoracic spinal segments and may radiate to the shoulder and down the arms thus simulating coronary disease.

Heart pain is usually referred along the 5th cervical through the 4th thoracic spinal nerves. Corrective evaluation is had by painstaking history, roentgenograms and electrocardiograms. There is a tendency of gallstones in biliary disease to co-exist with heart disease particularly after the age of 50 but as you just heard today it might co-exist from 30 on. Nerve stimuli originating in the gallbladder or the common duct may alter the flow of blood through the coronary arteries. Damage to the heart from biliary disease is often reversible if it is corrected early. The decision for major operation on the biliary tract, however, must be made judiciously as fatal coronary occlusion may occur during or soon after the operation. Nevertheless with the good anesthesia at our command today and with improved surgical technic the patient with coronary heart disease will frequently tolerate very well an operative procedure and will be benefited greatly with relief of symptoms. Many of us know of patients who have been completely relieved of what was thought to be coronary heart disease following an indicated operation on the bile passages.

Some of the benefits of cardiac improvement following cholecystectomy may be attributed to rest in bed, weight loss, change in diet and other factors incidental to the operation. I believe much credit should be given to the removal of diseased gallbladder or correction of biliary tract disease including the interruption of the nervous system of the cystic and common ducts which might initiate the stimuli which may account for the heart symptoms. This is the crux of our presentation, the nervous system of the gallbladder, cystic duct and common duct. The commonest sign of gallbladder disease is obstruction of the duct by stone or inflammatory edema and consequent changes in the biliary tree and liver. The extent of the damage will depend upon the degree and the duration of the obstruction. To my mind there is no such thing as a silent gallstone or an innocent gallstone. They may be sleeping dogs. There are some patients that come to us later after the lapse of 5, 10 or 15 years suffering with coronary heart disease and who have a so-called silent gallstone and who now have developed obstruction of the cystic duct or the common duct thus making the operation much more hazardous. Because of this type of case it is my opinion that gallstones, if found, and when found, although they be symptomless, should be removed.

We are not, however, considering today the calculous gallbladder but rather the noncalculous gallbladder and what to do about it. As a rule I do not advise the removal of the noncalculous gallbladder as the results in these

cases are often disappointing and cause some of our surgical failures. There are some cases in which operation or exploration of the biliary tract is indicated although the roentgenogram does not show stones. I can recall several cases in which we reluctantly operated on the so-called noncalculous gallbladder with poor function and have obtained excellent results. In these cases we invariably follow Dr. Nathan Womack's<sup>2</sup> (and others') concept and strip the cystic duct of fatty tissue and its nervous mechanism and ligate as close to the common duct as is consistent with safety. We further strip the common duct of its fat and nervous mechanism at the junction of the cystic and common.

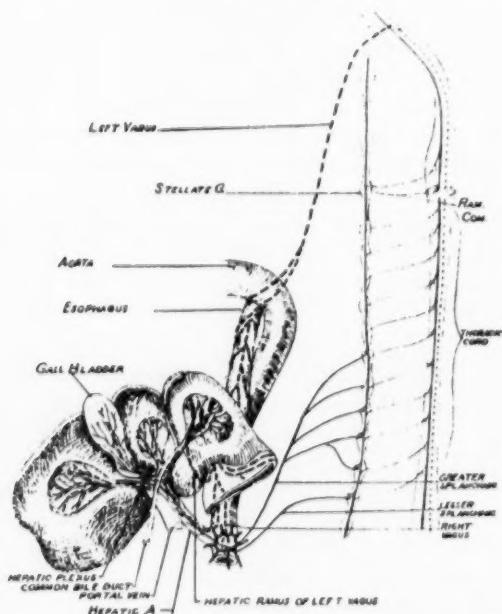


Fig. 1—Diagrammatic representation of the origin and gross distribution of the sympathetic and vagus nerve supply to the biliary tract and liver (After Kuntz).

Many of these noncalculous gallbladders will have common duct and pancreatic pathology ranging from stones in the duct to a stricture of the sphincter of Oddi and in these cases we open the common duct and dilate the sphincter by probes or by transduodenal direct vision. One should, however, be very sure before operating on the noncalculous gallbladder that all means of examination have been satisfactorily carried out and elimination of all other possible sources of the patients' complaints are thoroughly investigated.

I must confess that in doing common duct surgery I have sometime had great difficulty in determining what is inside of the common duct. Many of

the ducts containing stones will be dilated and you will not be able to palpate these stones. I agree with Dr. Feeney of Baltimore, whom I heard speak on this subject many years ago. He was firm in saying that you cannot tell what is inside the gallbladder by the feel of it; I feel the same way about the common duct. I don't believe in opening the common duct unnecessarily but if you have symptoms that warrant it and your findings are negative until you get to the common duct then I believe it should be opened, explored and drained.

In these cases we look for periductal disease and frequently find it around the cystic duct. Your patient may have had an acute attack of cholecystitis with edema and inflammatory reaction around the ligament which may subside and you may find a very acutely distorted cystic duct with adhesions.

According to Womack's theory, which he has worked out in many cases and with which we have tried to work along because it is interesting, in these inflammatory reactions around the cystic duct, the common duct and the gallbladder you find quite a bit of fibrosis. You get a certain amount of scarring all through it and in time it can perpetuate the gallbladder syndrome.

We know further that disease of the ampulla of Vater or the sphincter of Oddi can also give you biliary colic and biliary symptoms and we frequently open these common ducts to probe the sphincter. If it probes sufficiently well, well and good, and if not we open the duodenum and approach it from the inside and we are amazed sometimes to find out what pathology we would have left behind if we had not opened the duodenum.

I have two cases in mind at this moment which occurred two months ago or more. We were ready to close but the medical man was insistent on the symptoms. We opened the duodenum and found crustation and a stone in the ampulla but not a complete obstruction. The patient had a history of a short period of jaundice and that is why we operated on her. It is true that she had a noncalculous gallbladder but on the other hand she had biliary tract disease. It took some time to ream out this calculus and remove it.

Several years ago some of our patients had biliary dyskinesia postoperatively and after I say what I have in mind you might agree that you may have biliary dyskinesia following surgery. If we follow the concept of the nervous mechanism about the gallbladder, cystic duct and common duct we know that after operation on a case of biliary tract disease or particularly gallstones, that a given percentage of these patients are going to have so-called postoperative biliary dyskinesia. Why do we have it? We know that most of them have residual pathology. Some of them will have stones left in the common duct or they will have disease of the sphincter of Oddi. Now, excluding these obvious conditions, what would cause pain after operation?

Dr. Womack has done several re-operations in which a long cystic stump with considerable fibrosis was found, with or without stones. By removing the

stone from the cystic duct, if present, removing the fibrous tissue, and stripping it down to the common duct junction he has had almost 90-95 per cent complete relief of dyskinesia.

This type of case does not come on immediately postoperatively. It takes several weeks and sometimes months for dense fibrous tissue or neuromas to form.

The nerve supply of the biliary tract, including the liver, is derived from the sympathetic, vagus and phrenic nerves (Fig. 1). The majority of the nerve fibers to the biliary tree come from the sympathetic system and these fibers are derived from the greater and lesser splanchnic nerves, rami from the phrenic and vagus nerves join in with the sympathetic nerves. According to Raigorodsky

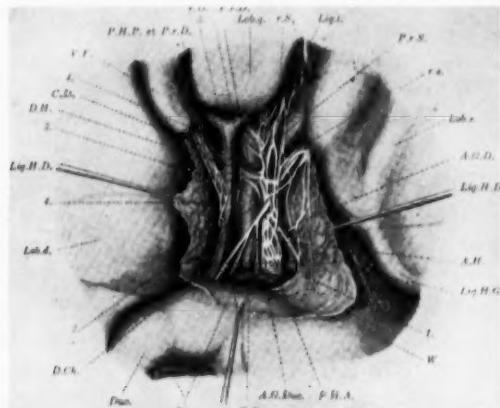


Fig. 2—Preparation of an adult with normal topographic relations seen from in front. Lob.s.—left lobe of liver; Lob.d.—right lobe of liver; Lob.q.—quadrate lobe of liver; Lig.t.—lig. teres; W.—stomach; Duo.—duodenum; Pn.—pancreas; Lig.H.G.—hepatogastric ligament; Lig.H.D.—hepatoduodenal ligament; A.H.—common hepatic artery; A.G.D.—right gastric artery; A.G.Duo.—gastroduodenal artery; r.D.—right branch of the hepatic artery; r.S. and r.Sl.—left branch of the hepatic artery; V.P.—portal vein; P.H.A.—anterior hepatic plexus; P.H.P.—posterior hepatic plexus; 1—nerves with the right gastric artery; 2.—anastomosis between the anterior and posterior hepatic plexus; 3.—lateral nerve of the gallbladder; 4.—cystic duct; 5.—medial cystic nerve (After Raigorodsky).

(Fig. 2) the hepatic plexus is divided into anterior and posterior portions and the two anastomose with each other by ramifications along the common duct, hepatic artery and portal vein. The medial nerve of the gallbladder which comes from the anterior plexus passes over the anterior surface of the common and hepatic ducts, anastomoses to the posterior hepatic plexus in the triangle formed by the cystic and hepatic ducts and goes along the medial surface of the gallbladder. The lateral nerve of the gallbladder comes from the posterior portion of the plexus and passes along the lateral surface of the common and

cystic ducts to the lateral surface of the gallbladder. One can readily see the delicate network of fibers along the common duct and these fibers are more numerous in the region where the cystic duct joins the hepatic or common duct.

Time does not permit detailed anatomical discussion of this picture but one can readily see the importance that we are placing on the nervous mechanism of the common and cystic ducts, particularly at their junction, as well as that of the gallbladder. The distention of the ducts sometimes causes severe epigastric distress, frequently vomiting. This is readily demonstrated when a "T" tube is placed in the common duct and irrigated after the patient is ambulatory. It seems logical that stimulation of the nervous system in the portal area would cause epigastric distress and similar symptoms are present before cholecystectomy.

Rather than talk too long on this subject I will close here and hope to get some questions from the audience.

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#### DISCUSSION

*Dr. Nathan Brodie (Brooklyn, N. Y.):*—I should like to ask Dr. Claud if in biliary dyskinesia, do the following factors reduce or increase the incidence: 1. mass ligation of the cystic duct and artery using one ligature; 2. the use of unusual care in ligating the cystic duct and artery.

*Dr. Claud:*—The question is whether these factors will reduce the incidence of biliary dyskinesia? The first was the old surgical procedure of mass ligation of the cystic ducts and structures as compared to the modern treatment of individual and careful identification of the cystic duct and structures. I believe mass ligation of the cystic duct and cystic artery involves more risk to developing postoperative dyskinesia. In answer to the second part of the question by Dr. Brodie, I believe meticulous dissection of the cystic duct and artery down as close to the common duct as safety will allow and the dissection should include the stripping of the cystic duct of its fatty tissue and nerves of this area, this procedure lessens the incidence of postoperative biliary dyskinesia.

*Dr. Brodie:*—How about trauma?

*Dr. Claud:*—Trauma is certainly an added factor. There is no question in my mind that in doing this type of surgery, one has to be careful of dissection and cause as little trauma as possible. I believe that in opening the common duct Allis clamps should not be used. We use guy sutures of fine chromic catgut which are tied later as part of the closure around the "T" tube in the common duct.

*Dr. Joseph Shaiken (Milwaukee, Wisconsin):*—My question is directed to Dr. Berk. What has been your experience in regard to chronic relapsing pancreatitis in the noncalculous gallbladder? Is there any relationship between these two diseases?

*Dr. Berk:*—I have found chronic relapsing pancreatitis more in association with alcoholism and excessive alcoholic intake than with associated biliary tract disease. When biliary tract disease exists it should be eradicated and corrected just as it would be if pancreatitis were not associated. I can recall at least one patient with chronic relapsing pancreatitis who also had mild noncalculous disease of the gallbladder; cholecystectomy was done as an elective procedure and the patient has now been symptom-free for about 1 year.

Of interest in this connection is the report from Boston which appeared not long ago in the *New England Journal of Medicine*\*. People who had had one or more episodes of acute pancreatitis were followed to see what happened afterward. It was found that those who had undergone cholecystectomy, whether or not the gallbladder contained stones, fared best of all. While these observations are highly interesting, it is not at all clear to me why removal of an apparently normal gallbladder should favorably affect the future course of an individual who has had one or more episodes of acute pancreatitis.

*Question:*—Would it be dangerous to use intravenous cholografin during an acute attack: 1. if only the gallbladder were suspected; 2. in the differentiation between gallbladder and heart disease, if not certain; and, 3. could any diagnostic benefit be derived from such a procedure?

*Dr. Berk:*—Unfortunately, I have not had much experience with cholografin in acute cholecystitis. Our studies were confined to other types of cases and our supply of material was limited. However, if I were confronted with a situation such as described in 1, I would not hesitate to use it for fear of danger from its use.

With respect to 2, if there were doubt in my mind whether the individual was suffering from acute cholecystitis or damage to the heart, I would be much more conservative. I would prefer to err in favor of cardiac disease and do nothing that might be harmful.

Whether or not information of value could be obtained from cholografin study of the gallbladder and ducts in the presence of acute cholecystitis, would depend to a large extent on the morphologic changes which have occurred. If the process is the result of a stone impacted in the neck of the gallbladder at its junction with the cystic duct, as is so commonly the case, the gallbladder would probably fail to visualize. The chances of seeing the ducts would be

\*Raker, J. W. and Bartlett, M. K.: Acute Pancreatitis; The Fate of the Patient Surviving one or more Acute Attacks. *New England J. Med.* **249**:751, 1953.

better; indeed, intravenous cholografin study in these circumstances might disclose stones in the ducts in some cases.

*Dr. W. Stuart Henderson (Akron, Ohio):*—My questions are directed to Dr. Berk.

In the nonjaundiced patient, if the gallbladder is not visualized even after repeated dose, what success has there been with cholografin intravenously? In what per cent of patients has Dr. Berk found that cholografin was contraindicated because of allergic reaction? Would he recommend it as a routine procedure if the gallbladder were not visualized?

*Dr. Berk:*—Every subject is not only questioned beforehand about iodine sensitivity, but each is also carefully tested before the material is given. We have used intravenous injections of 1 c.c. for the latter purpose. Some of the material may be injected into the conjunctival sac or into the skin instead. There will be some persons to whom the material cannot be given because of obvious sensitivity. Thus far, we have been fortunate enough not to encounter a serious sensitivity reaction. I have no doubt, however, that with increasing use of the material, such a reaction will occur.

We are currently engaged in studies designed to try to find some answers to the questions regarding the role of intravenous studies in patients whose gallbladders fail to visualize after oral technics. We have encountered several instances of successful visualization after intravenous cholografin when there had been no visualization after oral media. We are not certain at the moment, however, that this indicates that the gallbladder is normal. Ability to concentrate the contrast medium is much more a factor after oral media than when concentrated contrast material is given intravenously. Perhaps the failure to opacify after oral media reflects a defect in concentrating function which may not be as apparent when the contrast material is given intravenously.

*Dr. Victor Willner (New York, N. Y.):*—There were some reports from Europe that they have had agranulocytosis following the introduction of this material.

*Dr. Berk:*—I was informed that such a situation was observed in one patient in another institution in Philadelphia. The hematological alteration, however, was transient and it was not certain that the contrast medium was responsible. We are not aware of similar occurrences in any of our subjects, but we have not routinely performed blood counts before and immediately after administration of the material. In no subject, however, has there been anything clinically to suggest significant hematological alteration.

*Dr. Cecil Mantell (Staten Island, N. Y.):*—Is it sound procedure to do a gastrointestinal series immediately following cholecystography?

*Dr. Berk:*—I know of no reason not to perform both examinations.

*Dr. Donald C. Collins (Hollywood, Calif.):*—May I add a little to this discussion? Among surgeons the problem of what constitutes the proper treatment of acute cholecystitis is still a matter of considerable controversy and indecision. Personally, I take the position that if the patient can be tided over safely with supportive treatment, and if he continues to improve; then that particular patient should be postponed until such time arrives when you can perform a thoroughly complete operation. Usually a cholecystectomy is fraught with considerable danger unless that particular patient is operated upon within the first 24 to 48 hours after the initial onset of symptoms. Later than this, usually, one cannot safely explore nor identify the common duct and its accompanying structures. Most instances of acute cholecystitis present themselves more than 48 hours following the onset of their acute disease.

I think conservative, nonoperative, symptomatic management is indicated when your patient remains in good condition and demonstrates progressive improvement. Such a treated patient should be seen twice a day by you on the surgical service in the hospital until the acute inflammation has thoroughly subsided. The question of what constitutes an adequately safe period of delay has as yet not been completely settled nor agreed upon. I like to wait six to eight weeks before operating. In the interim I fervently hope that this individual patient will not develop another attack of acute cholecystitis. In a few instances, I have been forced to perform an emergency laparotomy much earlier, because of the failure of that one patient to improve on conservative medical management in the hospital. Frequently in such instances I have commonly encountered marked edema of the tissues and subsiding phases of an acute inflammatory process that greatly obscures anatomical landmarks and renders a cholecystectomy a procedure fraught with considerable danger.

## GROWTH-PROMOTING EFFECTS OF ANTIBIOTICS\*

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It has long been thought that the microorganisms of the digestive tract might have something to do with nutrition, and Pasteur once postulated that they might be necessary for life. Modern experiments at Notre Dame show conclusively that germ-free animals can function well, but there is also a considerable body of evidence indicating that microorganisms may have a very profound influence on nutrition.

Microorganisms, like other forms of life, contain elaborate systems for biochemical processes, and these systems involve the B vitamins. So far as analyses have been carried out, all microorganisms seem to contain all of the common B vitamins. Yet many of them are able to grow on very simple media, devoid of vitamins. The conclusion reached under these circumstances is that the vitamins within the microbial cell have been synthesized by the microorganism itself.

There is much evidence that the microorganisms of the digestive tract synthesize vitamins. When relatively deficient diets are fed to rats, the intestinal contents often contain larger amounts of a B vitamin than the diet, and balance experiments show larger amounts excreted than ingested. Diets completely devoid of certain vitamins such as folic acid or Vitamin K fail to produce symptoms of deficiency in the rat, although such symptoms develop readily when changes in intestinal microorganisms are induced by the inclusion of appropriate sulfa drugs in this diet.

The discovery that antibiotics can increase the growth of animals came about as an extension of this latter type of experiment. When antibiotics became available, it was thought that they, like the sulfa drugs, might intensify the effects of a dietary deficiency. A group of investigators at Wisconsin, however, reported in 1946 that rats fed a purified diet containing streptomycin grew better than control rats, and this result was attributed to an alteration in the microorganisms of the intestines.

The real stimulus to the current use of antibiotics in animal feeds came from the observation that fermentation residues contain Vitamin B<sub>12</sub>, and that some of these residues produced more growth in chicks than could be explained on the basis of the Vitamin B<sub>12</sub> present. The mold studied happened to be one that produces aureomycin, and fractionation of this fermentation residue for the apparent "new growth factor" yielded the surprising result that the growth

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promoting factor was aureomycin itself. Subsequent developments followed logical lines and a number of different antibiotics were found to be capable of stimulating growth. This is now the basis of a large industry, and antibiotics seem to be particularly valuable for swine and poultry.

The slides illustrate the magnitude of the effect, and also the fact that the effectiveness of an antibiotic quantitatively varies inversely with the completeness of the diet. The growth of laboratory rats fed a complete synthetic diet is not greatly affected by penicillin or aureomycin, although these antibiotics may cause very marked increases when the diet is suboptimal in one of the essential B vitamins.

A summary of 187 experiments from several different laboratories indicates the usual stimulation in swine fed crude practical diets to be about 10 per cent, with considerable differences between antibiotics. This increase in growth may involve a real economic advantage, since the amount of feed required per unit of gain goes down when the growth rate is increased.

It should be pointed out that the concentrations of antibiotic necessary to stimulate growth are very much less than those used in medicine; as a rough estimate the amounts range from two-tenths to five per cent of those necessary to produce clinically useful concentrations of antibiotic in the blood.

When antibiotics are fed, the changes which take place in the intestinal population are of a number of types. There may be a decrease in harmful, toxin-producing strains of organisms, e.g., in the numbers of *Clostridium perfringens* in the lower digestive tract of birds fed antibiotics.

A shifting in the types of organisms may also result. In general there is a decrease in anaerobes and in lactobacilli, and an increase in coliforms. It so happens that many lactics and anaerobes require a more specialized and complete medium for growth than the coliforms, many of which grow on a very simple medium.

This shifting in population is capable of producing two results of nutritional importance. The organism which is favored, the coliform, can synthesize some of the vitamins that happen to be limiting in the diet. On the other hand the lactobacilli tend to absorb into their own cells vitamins from the digestive tract and effectively withhold them from the host. These organisms are suppressed in this process.

Then, as one would expect, there are marked increases in antibiotic-resistant types of organisms. This latter phenomenon has already had clinical significance, as the slides show. With the continued use of an antibiotic in the amounts necessary for therapy, strains resistant to that antibiotic have developed, and therapy that once was successful in a high percentage of cases now no longer is very effective.

So far there do not appear to be comparable losses in the potency of penicillin or aureomycin as far as the growth of animals is concerned. Perhaps this is because the concentrations used in practical nutrition are low. Nevertheless, in time one may expect the appropriate resistant strains of organisms to predominate in the bodies of domestic animals, and then the antibiotics now in use will have to be replaced by others.

#### DISCUSSION

*Dr. I. Snapper:*—The interesting facts which my previous compatriot has reported, are also of practical importance for medicine. After the war, one of my associates, Dr. Max Ellenberg, published that he had successfully treated amebic dysentery with sulfa drugs. I must confess that at the time I doubted whether this observation was completely correct. Soon afterwards, however, it became evident that many other antibiotics, especially aureomycin and terramycin also have a favorable influence upon intestinal amebic infections. These substances have only weak amebicide action. However, they kill the anaerobic *Clostridia* on which the amebae feed. This, therefore is an indirect effect on amebiasis which acts in intestinal amebiasis but has for apparent reasons no influence in amebic hepatitis.

Many observations have been made in the course of the centuries which either have been forgotten or which nowadays are considered to be just fairy tales. In some instances our hypercritical attitude has been proved to be incorrect and centuries later the importance of the forgotten "ridiculous" reports became suddenly evident. When the Chinese recommended the chewing of the leaves of a specific tree in order to heal asthma, the foreigners thought one could just as well eat powdered dragon teeth. Later it was proved that the leaves of the ephedra tree actually contain the antispasmodic ephedrine which since then has become popular in the Occident. Therefore, occasionally the so-called old wives' tales may come back with a vengeance.

Now, as our incomparable Dr. Wangensteen mentioned yesterday, Arbuthnot Lane, a surgeon of Guys Hospital who later degenerated to a medical writer in the daily gazettes, performed colectomies to treat the most divergent diseases from constipation to exophthalmic goiter and arthritis. How did he come to this? He had read the famous Metchnikoff, who explained the longevity of the Bulgarian people by their custom of drinking kefir milk, nowadays known as yogurt. Metchnikoff held that under influence of kefir milk the flora of the intestine was changed and that thereby the span of life in the Bulgarians was considerably increased. This for Arbuthnot Lane was the justification of his panacea—the colectomy.

Today we here have heard what a change of flora of the intestine can do to the growth of animals. We may now start to speculate that Metchnikoff may well have been right in assuming that in humans a change of flora of the colon can increase longevity.

## RECTAL PROBLEMS\*

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In this presentation of rectal problems, I should like to confine my remarks to those disorders associated with trauma and to include the lower sigmoid colon as essential to this discussion. A brief review of the embryology and anatomy of the distal alimentary tract appears to be of value as an introduction to the subject matter.

During normal fetal development there is a caudad extension of the entodermal hindgut which unites with an ectodermal invagination of embryonic proctodeum. The membrane or anal plate thus produced at the level of the dentate line later disappears and anorectal continuity is thus established. In the event that any maldevelopment occurs, one may readily appreciate the innumerable varieties of congenital anomalies that could result.

The anus extends from the verge externally up to the dentate line and is covered with squamous epithelium. It serves as a sphincter-controlled exit to the alimentary tract. The sensory nerve supply is somatic in character and perception to heat and pain stimulation is severe. Aside from an occasional impalement injury, and the very rare birth damage to the sphincter which has been neglected, most trauma to the anus with resultant incontinence is the aftermath of previous surgical procedures with inadvertent damage to the sphincter. Injuries to the anus and their management constitutes more of a discussion than would fit the scope of this presentation.

The rectum, extending from the dentate line up to about the level of the third sacral vertebra where it joins the sigmoid colon, is about 15 cm. long. The mucosal lining is made up of columnar cells. In the rectum, except for the valves, this lining is smooth but becomes thrown into folds in the lower sigmoid. This lower segment of the intestinal tract serves as a storage vestibule. The distal rectum is extraperitoneal while the proximal half is partially intraperitoneal. In the lower sigmoid, the bowel is covered with peritoneum except at the root of the mesentery. One may recognize that any penetration of the distal rectum would most likely be extraperitoneal while in its proximal half it could either be intra- or extraperitoneal. As the level of the lower sigmoid is reached, a perforation would most likely be intraperitoneal; but, by occurring between the layers of the mesentery, it could possibly be extraperitoneal. The sensory nerve supply of the rectum is visceral and pain or discomfort is not

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elicited by incision or fulguration but rather by distention or spasm. The rectosigmoid may be injured as part of a generalized severe trauma in which numerous other structures are damaged. Other injuries such as a severed vessel may require earlier and more constant attention than the injury sustained by the rectosigmoid. The rectum or lower sigmoid is occasionally the sole site of injury, and it is to this type of situation that I would like to refer. By so doing, one can give the basis for the management of all rectosigmoid injuries whether they be part of a generalized severe trauma or the only manifestation of the trauma.

Injuries to the rectum and lower sigmoid, in some cases, result from carelessness and/or poor judgment; however, many are unavoidable. Unlike in wartime when rectosigmoid injuries from external violence are common, they are not often seen in civilian practice. As an etiological agent, the enema or irrigation, the foreign body, or the proctoscope is to civilian life what the bullet or shrapnel was to warfare practice in causing rectosigmoid injuries.

Little can be done to prevent the enema or irrigation and the foreign body injuries, but the frequency of trauma by the proctoscope can and should be reduced. When one considers the rectosigmoid polyp as a precursor to cancer, it is good news that a tremendously greater number of these polyps are being discovered now in contrast to a decade ago. Since there is no reason to believe that there has been a sudden increase in the development of these polyps, their increased discovery is the result of conscientious physicians examining this blind and potentially dangerous segment.

The proctoscope has become an instrument for use by all physicians. No longer is its employment for diagnosis limited to a small group. By including a proctoscopic study as an essential part of every physical examination, we are in an excellent position to practice good cancer prevention and early detection.

We recognize certain dangers associated with the proctoscope and have made instructions in its use available to all of our house officers. It is hoped that at least some of the injuries to the rectosigmoid resulting from proctoscopy may be avoided by an intense program of thorough and widespread instruction to all who are occasioned to use the instrument.

When one considers the symptoms that may indicate trauma to the rectum, it is disappointing to find that they may be quite slow in their development. Discomfort is not too uncommon, but early, true pain may be somewhat unusual. This can be explained on the basis of the visceral sensory nerve supply to the rectum, as true pain results from distention, pressure, etc., while incision, crushing, puncturing, or fulguration give rise to little or no discomfort. On the other hand, the anal segment, which has the somatic sensory nerve supply responds to a stimulus; and severe pain is produced. The lack of pain in the rectum has been one of the bad features in delaying the early detection of

rectal carcinoma. These lesions may go undetected if there is no evidence of an obstruction or a discharge, or unless routinely examined by a physician.

A through-and-through gunshot wound of the rectum has the external findings plus the pain associated with the missile traversing other tissues, and therefore the diagnosis is not extremely difficult. Injuries to the rectosigmoid can and do take place, and physicians should be ever mindful of the possibility of an injury occurring during various proctologic, diagnostic, or therapeutic procedures.

The earlier symptoms of trauma to the lower sigmoid and rectum are not characteristic. Pain may be absent or slow in development. Bleeding, if present, may vary from a minimal amount to a profuse hemorrhage. Shock frequently appears but depends greatly upon the extent of the injury and tends to become more severe with the elapse of time.

Discomfort, bleeding, and the onset of shock are probably the earliest signs and symptoms associated with rectal trauma. Nausea, vomiting, distention, fever, rapid pulse, etc., may occur later as a result of complications, such as peritonitis, which may have developed.

A complete history, careful physical examination, scout x-ray picture of the abdomen, proctoscopic direct vision, and being very suspicious that an injury has occurred whenever the possibility exists will all aid in the establishment of a reasonably early diagnosis. An early diagnosis is of paramount importance, because morbidity and mortality usually increase with delay. A negative scout film may be of little value, but the presence of ectopic air, be it intra- or retroperitoneal, is of great significance.

In general, the management of injuries to the rectosigmoid may be considered as consisting of one or a combination of two or more of the following principles:

1. Removal of etiological agent, if present.
2. Repair and/or debridement of damaged tissues.
3. Create drainage.
4. Establish fecal diversion.
5. Search for and begin early management of any complication.

Many cardinal principles of care are listed but only rarely will it be necessary to perform all of them. For separate consideration each principle may be best understood if an illustrative case history is reviewed.

All principles were employed in the treatment of a young male patient, J. M., who was accidentally shot in the buttocks and lower abdomen. In addition to the rectal injury he sustained trauma to the bladder and pelvic bones. Even

though the bullet had passed into and out of the patient, it had left a trail consisting of fragments of bones and clothing, some of which were picked from the tears in the rectum. Devitalized tissue was cut away and closure of the rectal wounds accomplished. Postanal external drainage, even though of questionable value, was carried out. A complete fecal diverting transverse colostomy was performed. Forty-eight hours later, a search for the cause of a temperature elevation to 39.6°C. was rewarded by the discovery of atelectasis which responded promptly to therapy.

This type of management of rectal injuries is certainly the exception rather than the rule, because this form of injury constitutes only a small percentage of all rectosigmoid trauma.

It has been previously mentioned that treatment may consist of applying only one of the cardinal principles. In going over each principle, an illustrative case discussion may aid in clarification.

*1. Removal of etiological agent, if present:*—This principle is necessary primarily in the management of foreign bodies. It is a general feeling that only a very small number of objects found in the rectum arrive there as a result of being swallowed or accidentally misplaced there during some form of treatment. The great majority of foreign bodies in the rectum, which may be of all sizes, shapes and types, usually are placed there either purposely or accidentally by the patient for reasons best known only to themselves. Possibly the incidence is somewhat greater among inmates of penal and mental institutions.

To accomplish this principle of removal of etiological agents, one may be faced with the task which on occasions may severely tax his ingenuity. The removal is occasionally quite traumatic, particularly if the object is made of glass, in which case breakage could change a reasonably insignificant situation into a very real problem.

Almost as many methods as one could imagine have been suggested for the purpose of extracting foreign bodies. In less than a year at a penitentiary hospital, two patients were treated for rectal foreign bodies. One was a spoon which had been introduced by the patient. The other was a short piece of broom handle that had been introduced forcibly by fellow prisoners during mass shower time. Each was removed with relative ease, and no anesthetic was required. The second foreign body would possibly have been passed spontaneously at a later time, but because of the circumstances surrounding the introduction, immediate extraction was deemed wise. An anesthetic is of tremendous value as an aid in foreign body removal and should be used whenever cooperation by the patient or ease of removal of the object is at all questionable.

*2. Repair and/or debridement of damaged tissue:*—This step is frequently required along with some other of the principles, but occasionally it is all that need be done. A patient, while undergoing proctoscopy, made a sudden unex-

pected motion. The examiner promptly realized that the sigmoid had been lacerated. The scope was withdrawn and arrangements were made for hospitalization and immediate operation. A laparotomy was performed with simple closure of the defect in the bowel wall. Recovery was rapid and complete.

It was observed at operation that there had been minimal fecal contamination of the peritoneum. This is because the lower bowel, as is the case of all proctologic examinations, had been cleansed. Antibiotics were administered as a precaution, but this was probably unnecessary.

3. *Create drainage*:—This procedure is of questionable value, but continues to be employed in conjunction with some of the other measures. One method consists of draining the presacral space through the postanal perineum, with the hopes of preventing the development of a retroperitoneal phlegmon. Some form of drainage may be occasionally necessary as in the case of a patient who after a day of perineal discomfort developed a large abscess which was promptly drained. This abscess was not considered to be at all unusual until it was found to have been caused by a large piece of fish bone which was encountered in the pus.

4. *Establish fecal diversion*:—A colostomy should be performed whenever viability of tissue and/or satisfactory closure of the bowel is questionable. We have recently had two occasions to employ this as the sole method of management.

One patient, an elderly male, while in the hospital undergoing a routine work-up to ascertain the cause of recent abdominal discomfort, and mild rectal bleeding, underwent a proctoscopic examination in the late afternoon. The scope was introduced to 25 cm. and above this level the wall appeared edematous and a small amount of blood was observed. The instrument was withdrawn and the patient was scheduled for barium enema study the following morning. A scout film of the abdomen revealed a large amount of extraperitoneal air which extended up into the mediastinum and the neck. Crepitus could be felt. The patient's general condition was good but exploratory laparotomy was considered wise. At operation, it was discovered that a diverticulum, located between the layers of peritoneum in the root of the mesentery had "blown out". A transverse colostomy was performed. The "air" which was felt to consist chiefly of atmosphere introduced under pressure by the bulb rather than intestinal gases, soon absorbed. At no time did the patient appear ill.

The other patient, also a male, who had been on a drinking spree and became unruly, was given what was later repeatedly alleged to have been paraldehyde per rectum. When first seen several hours later, after he had sobered up, there was rectal pain and bleeding. Even though unable to prove it, the necrotic appearance of the lumen of the bowel made us suspicious that formaldehyde had been mistakenly introduced. By defunctionalizing the bowel

with a transverse colostomy, recovery took place and later the colostomy could be closed.

This might be an opportune time to mention that the closure of temporary colostomy should not be delayed indefinitely. This brings to mind two individuals, both of whom had colostomies in the treatment of trauma. One lesion was from a gunshot wound and the other was from surgical damage to the sphincter with resultant incontinence. When first seen, these patients had both had their colostomies performed over two years before. After repair of the damaged sphincter, and the voluntary decision by the other patient to have the colostomy closed, closure was performed on both. This was carried out, however, only after careful preparation of the long defunct segment of bowel. First, a barium study was made to assure against any obstruction. Following this, the function of the bowel was stimulated by the daily introduction of a pastry mixture of barium into the proximal end of the distal segment. It was only after definite assurance was obtained that the inert bowel had regained function that operation was performed. These precautions are the result of having observed a patient several years ago in whom there was a near fatal outcome. This resulted from re-establishing continuity with a long unused segment of bowel which failed to function with subsequent development of ileus and peritonitis.

5. *Search for and begin early management of any complication:*—A patient was recently observed upon whom an abdominoperineal resection had been performed. About a month following operation, the patient experienced some difficulty in performing an irrigation. When he used more force there was a sensation of something "giving way" and some slight pain. He was re-hospitalized and a scout x-ray film was taken, which was negative. It was elected to observe the patient. He developed several abdominal wall abscesses which were drained and recovery followed.

The above is quite different from another patient who had undergone partial colectomy for ulcerative colitis. During a routine retrograde barium study it was discovered that most of the barium had entered the peritoneal cavity. An immediate ileostomy and peritoneal toilet was performed. The remaining diseased colon was removed at a later date.

One may observe that there are no clear cut characteristic signs or symptoms which are indicative of rectosigmoid trauma. Neither is there an established set of rules to govern the management of these injuries. Each patient in whom the possibility of such an injury is present becomes a problem of early diagnosis and individualized treatment.

#### DISCUSSION

*Dr. O. H. Wangensteen:*—Those of us who have remained to the end of this program, I am certain, feel amply rewarded by having had the opportunity

of hearing this nice enunciation of the principles in the treatment of unusual conditions of the rectum.

It is rather unusual to have someone list as a title for his talk "Rectal Problems" and not speak of fistula-in-ano, hemorrhoids, or cancer. In a way I am glad that Dr. Gerwig did not choose to enunciate hemorhoidectomy. Whereas this is a good operation under certain circumstances, I have a feeling in the years that lie ahead we shall see a lesser number of hemorhoidectomies being done without good indication. If in your hospital there are surgeons who do not affect a primary interest in proctology, and you observe that these men are listing many hemorhoidectomies each month for operation, I suspect you will find they are doing a lot of unnecessary surgery, at least they are performing hemorhoidectomy on very slight indication.

Uterine suspension is another such operation, which by general agreement is being consigned to the limbo of forgotten operations. That is the ultimate and final resting place for all unnecessary operations.

## CASTROINTESTINAL HEMORRHAGE: THERAPEUTIC EVALUATION OF BIO-FLAVONOIDS\*†

REPORT ON 55 CASES

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The important part played by the capillary system in blood circulation is fully recognized. Our knowledge of the morphology of this system, first mentioned by Galen (131-201 A.D.) in his book *De Usa Partium*<sup>1</sup>, is quite complete. Yet its pathology and its etiologic role in disease only recently became the subject of extensive experimental investigations and clinical trials. Gradually, we became cognizant of the fact, which for a long time somehow evaded our attention, that it is in the capillaries that the essential work of the circulatory system is carried on and that any deviation in capillary functioning might contribute to existing localized or generalized pathologic conditions, or even might induce them. The striking fact concerning the pathology of capillaries is that various factors of neurogenic, bacterial or viral nature, or of chemico-toxic origin may induce increased capillary permeability and fragility, and might be responsible for capillary hemorrhages. The alteration in the capillary wall is present in almost all inflammatory processes as Krogh<sup>2</sup> and many others after him demonstrated. Duran-Reynals<sup>3</sup> has proved that the spreading factor or hyaluronidase increases capillary permeability, and Diller, et al<sup>4</sup> and others have demonstrated that bacterial polysaccharide can cause profuse capillary hemorrhage. In his review of the capillary syndrome, Sokoloff<sup>5</sup> pointed out that varying degrees of capillary injury are found in the majority of viral infections.

The gastrointestinal mucous membrane with its vast finely elaborated capillary network, appears to be particularly sensitive to the toxic factors which so often beset the digestive system of modern man. Osborn<sup>6</sup> stressed the fact that the gastric and duodenal arteries of all age groups are very nearly immune to the usual forms of arteriosclerosis. Thus, arteriosclerosis apparently cannot be blamed for gastric and duodenal bleeding. Small lesions of an inflammatory origin, with the capillaries altered were described in many cases of incipient gastric and peptic ulcer. Gray et al<sup>7</sup> in a series of pathologic investigations of removed portions of the stomach and duodenum revealed definite lesions as a potential source of bleeding. In most cases, these lesions consisted of small

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inflamed areas, ulcerated or not, with hemorrhagic spots around the capillaries. In massive bleeding, the capillaries were partially or completely destroyed and the precapillary arterioles were also involved.

"Gastrointestinal hemorrhage is encountered frequently," Judd and Hill remark<sup>8</sup>, "to be a real challenge to the medical profession." Peptic ulcer is one of the most common conditions with which the gastroenterologist of today is confronted. It is difficult not to agree with Boles and Westerman<sup>9</sup> that "we are still treating peptic ulcer blindly, and consequently with embarrassingly poor results." Opinion continues to shift between medical and surgical management. It is said that hemorrhage, either in the form of hematemesis or melena, occurs in 85 per cent of cases of ulcer<sup>10</sup>. In postbulbar ulcer, hemorrhage is particularly a frequent phenomenon, according to Swarts and Rice<sup>11</sup>. The gravity of hemorrhage in older patients affected with ulcer was stressed by Branwood and Robertson<sup>12</sup>, who emphasized that the presence of associated diseases might be a contributing factor. The mortality in this group from hemorrhage was as high as 20-22 per cent in the series of patients observed by Grant<sup>13</sup>. The follow-up of operated patients showed recurrence of hemorrhage within five years in 63 per cent of the cases according to Gray, et al<sup>7</sup>. Although Judd and Hill<sup>8</sup> and others give smaller figures for the recurrent hemorrhage in operated patients with ulcer, nevertheless, there has been in recent years a trend to treat an uncomplicated duodenal ulcer medically. On the other hand, gastric ulcer, because of the unpredictability of its behavior, especially when intractable, is usually treated surgically.

In view of the recent accumulative evidence that the hemorrhage in ulcer and other gastrointestinal bleedings might be due primarily to deficiencies of the circulation of intestinal mucous membrane, we embarked on the present clinical investigation, in which Vitamin P, or permeability factor, otherwise known as bio-flavonoids, were administered together with ascorbic acid\*.

The work of Armentano, et al<sup>15</sup>, Bacharach, et al<sup>16</sup>, Scarborough<sup>17</sup>, Griffith and Lindauer<sup>18</sup>, Sokoloff and Eddy<sup>19</sup>, and others, has established the specific activity of Vitamin P (bio-flavonoids), in regard to capillary fragility phenomena. The usefulness of citrus bio-flavonoids in certain hemorrhagic conditions, in which an increased capillary fragility was present, was revealed by many investigators. Thus Greenblatt<sup>20</sup> reported the therapeutic value of bio-flavonoids in habitual abortion, Rogers and Fleming<sup>21</sup> in the prevention of erythroblastosis, Biskind and Martin<sup>22,23</sup> and Sokoloff<sup>24</sup> in the capillary syndrome induced

\*The preparation used in this study was C.V.P.®, a mixture containing whole water soluble natural citrus flavonoid complex, and ascorbic acid. These bio-flavonoids, similar to, but not identical with, the substance isolated by Szent-Györgyi, which he designated Vitamin "P", have been described by Sokoloff, et al<sup>14</sup>. The commercial preparation, kindly supplied by the U. S. Vitamin Corporation, contains in each capsule 100 mg. each of flavonoids and ascorbic acid. Throughout this paper, dosage refers to the flavonoid component (100 mg. = 1 capsule).

by viral and bacterial infections, Saelhof<sup>25</sup> in ulcerative cystitis, Loewe<sup>26</sup> in retinitis, Jones and Croce<sup>27</sup> and Payne<sup>28</sup> in tuberculous hemoptysis, Arons, et al<sup>29</sup> and Martin<sup>30</sup> in radiation injury. Puig-Muset<sup>31</sup> and Sokoloff and Redd<sup>32</sup> on the basis of their histochemical investigations, suggested that bio-flavonoids have a specific affinity for the intercellular cement of the capillary wall, and thus their action apparently resulted in decreasing abnormal capillary permeability. In their experimental study, Eddy, et al<sup>33</sup> demonstrated that bio-flavonoids prevented hemorrhage induced by bacterial polysaccharide.

In our present studies, 53 patients with gastrointestinal hemorrhage, and two with epistaxis were treated with CVP.

The following case histories illustrate the effect of this therapy on bleeding.

*Case 1:—C-2902, W. H., male, 57 years of age, accountant.*

*Past History:—*In 1931, was operated for ruptured duodenal ulcer. December 1933, had tarry stools, pain in the duodenal area. Was x-rayed and told that he had recurrence of his ulcer.

Patient consulted us in September 1934 because of tarry stools and pain. His age at this time was 36, weight 120 lbs. and B.P. 120/62. He also suffered from recurrent attacks of hay fever and was allergic to certain foods.

Physical examination revealed marked tenderness in the upper abdomen, a postoperative hernia in the scar. Gastric analysis—free hydrochloric acid 10; total acidity 20, occult blood positive and mucus 1+; Urine—nothing remarkable; Blood count—Hgb. 84 per cent; R.B.C. 4,710,000; W.B.C. 6,250; Polys. 66, Lympho. 28, Eosin. 1, Mono. 4 and Baso. 1. Stool—with guaiac test showed positive occult blood. Patient was treated with diet and medication.

On March 29, 1937, patient complained of occasional blood in the stool. He had no gastric symptoms. Physical examination: Weight 124½ lbs.; B.P. 110/80; Hgb. 78 per cent; Stool hard—occult blood+. Rectal examination revealed an internal congested hemorrhoid and a superficial anal fissure, the source of the blood.

April 27, 1937—Weight 127½ lbs.; B.P. 120/80; Hgb. 78 per cent; Stool negative. May 25, 1937—weight 172½ lbs.; B.P. 120/80; Stool—negative; Hgb. 80 per cent. Dec. 4, 1944—Weight 128½ lbs.; Stools, tarry; Hgb. 78 per cent. Dec. 7, 1944—Stool still showed positive occult blood.

Patient felt well for 4 years. On Nov. 12, 1948, his weight was 138½ lbs.; stool negative; Hgb. 83 per cent. Had a bad summer due to his hay fever, was nervous, but otherwise had no ulcer symptoms.

Oct. 17, 1950—weight 134½ lbs.; stools tarry, mucus ++; Hgb. 66 per cent. Claims to have excited himself which brought on upper abdominal distress. Patient was sent into hospital where he was placed on an ulcer regime and given injections of coagamin. Nov. 3, 1950—Hgb. 70 per cent; R.B.C., 3,220,000; B.P. 125/80, was advised to continue diet and medication at home. Nov. 10,

1950—weight 136 lbs.; Hgb. 72 per cent; R.B.C., 3,690,000; stool—negative. Dec. 20, 1950—weight 142% lbs.; Hgb. 86 per cent; R.B.C. 4 million+; B.P. 120/80; no tenderness in upper abdomen, no pain, had slight bleeding from gums due to self imposed restriction of citrus fruit and vegetables. Was given ascorbic acid and other medication with good results.

Patient was not seen until July 12, 1952. He complained of weakness and apprehension, fear that he would get a hemorrhage and develop cancer. A thorough study including a galactose tolerance test failed to reveal anything serious. October 21, 1952—weight 140 lbs.; Hgb. 76 per cent; B.P. 130/85; gas; stool—negative. March 12, 1953—No intestinal complaints. B.P. 130/82; Hgb. 86 per cent; stool—negative. June 12, 1953—weight 137 lbs.; Hgb. 83 per cent; stool—negative; B.P. 140/85. Oct. 29, 1953—weight 141½ lbs.; Hgb. 92 per cent; stool—negative.

*Examination:*—Nov. 17, 1953—weight 139½ lbs.; Hgb. 83 per cent; complained of sweating, weakness, blood in the stools, slight epigastric pain, very nervous and jittery.

*Diagnosis:*—Ulcer with bleeding.

*Treatment:*—Referred to Polyclinic Hospital; diet and C.V.P., one capsule three times daily after meals. Nov. 22, 1953—stool negative and patient was sent home to continue C.V.P. capsules. Jan. 5, 1954—weight 138½ lbs.; Hgb. 83 per cent; B.P. 130/80; stool—negative. Dec. 27, 1954—weight 141 lbs.; Hgb. 83 per cent; B.P. 130/75; stool—negative. Continues taking C.V.P. Has no complaints. May 1955—came in for check-up. All findings were normal.

*Remarks:*—A case of ulcer of 24 years' duration, with repeated bleeding. CVP therapy instituted 8 months ago has had a salutary effect upon his condition. Bleeding stopped within four days.

*Case 2:*—D-3584, D. G., male, 67 years old, had a prostatectomy in 1950.

Consulted us on May 21, 1954—complained of pain in the epigastric area, lower bowel, vomiting and constipation.

*Physical Examination:*—Weight, 168½ lbs.; B.P. 170/92; marked succussion in stomach, palpation caused a feeling of nausea. Rectal examination—negative. A stomach tube was passed and several quarts of dark, foul smelling material were removed. The guaiac test was positive. He was admitted to the hospital for further investigation. A blood count showed Hgb. 74 per cent; R.B.C. 3,360,000. The stool was positive for occult blood (4+).

X-ray examination showed an immensely enlarged and dilated stomach occupying almost the entire abdominal cavity—6-8-24 hour residue present.

*Diagnosis:*—Cicatrized duodenal ulcer with marked gastric dilatation.

*Treatment:*—Daily lavage, intravenous glucose and vitamins, milk and jello diet plus 2 capsules CVP t.i.d. After several days, there was marked improve-

ment; the dark, foul smelling residue had disappeared, tests for occult blood were negative in the aspirated contents as well as in the stools. After three weeks, he was discharged. His weight at that time was 163½ lbs. He felt well, his appetite was good, and he no longer complained of acid eructation or vomiting. July 7, 1954—feels well, weight remained at 163½ lbs.; B.P. 140/80. He had no complaint except that he wanted to eat more. August 10, 1954—weight reduced to 157½ lbs. due to restricted diet; B.P. 138/80; continued diet and one CVP capsule after meals. September 23, 1954—weight 176 lbs.; B.P. 148/84; Hgb. 86 per cent; feels well, appetite good, continued CVP capsules and diet.

November 12, 1954—weight 174 lbs.; B.P. 100/88; feels well, no distress, advised to continue diet and CVP. In April 1955 patient developed a Bell's palsy, but no gastrointestinal symptoms.

*Remarks:*—A case of bleeding cicatrized duodenal ulcer with marked gastric dilation of considerable gravity which promptly responded to rest, daily lavage and a diet supplemented with CVP. The repeated bleeding which was present before CVP therapy has been absent for about one year.

*Case 3:*—D-3717, J. S., male, 54 years old, has suffered from ulcerative colitis for six months. During the past two months, 10 to 12 daily bowel movements, containing blood and mucus. Lost 20 lbs. in the two months.

*Examination:*—On September 24, 1954—weight 126½ lbs.; B.P. 124/80. Blood count: Hgb. 64 per cent; R.B.C. 3,820,000; W.B.C. 17,400; Polys. 72, Lympho. 26, Mono. 2; urine—negative.

*Sigmoidoscopy:*—Mucosa red, bleeding, numerous ulcerated areas. X-ray examination of colon—colitis.

*Diagnosis:*—Hemorrhagic ulcerative colitis.

*Treatment:*—Patient was placed on 2 CVP capsules t.i.d.—injections of 300 mcg. B<sub>12</sub> daily, for 3 successive days, then on alternate days; dihydrocortone tablets 20 mg. t.i.d.; Resion® and polymyxin, one tablespoonful t.i.d. and a high protein diet. The dihydrocortone tablets were discontinued after a week because of signs of fluid retention in the lower limbs and face (moonface).

November 3, 1954—B.P. 142/84; weight 151 lbs.; Hgb. 83 per cent; feels better, bowel movements less frequent and without blood. B<sub>12</sub> was continued once weekly and later at 10 day intervals. CVP capsules, one after meals with a tablespoonful of Resion and polymyxin once or twice daily.

January 3, 1955—weight 162½ lbs.; B.P. 140/90; stool formed and contained no blood or mucus. Diet was increased, avoiding roughage, CVP capsules continued because patient claimed that he felt better when he took them. Sigmoidoscopy showed an almost normal mucosa.

*Remarks:*—A case of bleeding ulcerative colitis which responded to combined therapy with Resion and polymyxin<sup>33</sup> and CVP. Bleeding was arrested promptly in spite of the fact that polymyxin has no hemostatic properties.

*Case 4:*—D-2088, N. M., female, 47 years old.

*Past History:*—February 5, 1951. Complained of nausea, blood in stool for three months, lost 3 lbs. in last 2 weeks. B.P. 130/80; weight 127 lbs. Palpation, marked tenderness was elicited along the descending colon. Stool examination—blood 4+, foul, large amount of bloody mucus. Blood count: Hgb. 86 per cent; R.B.C., 4,360,000; W.B.C. 12,500; Polys. 82, Lympho. 17, Mono. 1. Urine negative. Sigmoidoscopy—Numerous ulcerated areas with hemorrhage. Diet and rectal insufflation through a rubber catheter inserted into lower bowel, with a mixture of Kao-Lactos B, bismuth subgallate and barium sulfate, were instituted. March 2, 1951—weight 123 lbs.; frequent bowel movements containing some blood. Treatment was continued. March 29, 1951—she felt better; stool was formed and no blood present. April 12, 1951—Hgb. 90 per cent; no bleeding, 1 bowel movement daily, sigmoidoscopy was negative.

Seen again November 9, 1954—weight 122½ lbs.; Hgb. 88 per cent; B.P. 130/70. Was well until recently. Due to an emotional upset, there was a recurrence of diarrhea, with mucus and blood in the stool. She had developed a bursitis with calcium deposit of the left shoulder which was treated by a physician with cortisone. She again began to have diarrhea with blood in the stool. Sigmoidoscopy revealed numerous small ulcers, bleeding and pus.

*Diagnosis:*—Bleeding ulcerative colitis.

*Treatment:*—Resion and polymixin, ½ oz. every 4 hrs., also a tablet of Mycostatin, t.i.d. Nov. 14, 1954—there was only slight improvement. Nov. 22, 1954—Rectal insufflations and B<sub>12</sub> injections were given. Examined on Dec. 1, 1954—less diarrhea.

She was told not to go to work but she disobeyed and diarrhea and blood recurred. Patient developed a daily rise in temperature. She was admitted to the Polyclinic Hospital, where she remained for two weeks. Temperature ranged between 99° to 104°, with diarrhea and large quantities of blood and mucus. Sigmoidoscopy showed numerous denuded and ulcerated areas and pus. The blood count showed a marked anemia requiring transfusions, intravenous glucose and vitamins. X-ray of the colon showed a pseudopolypoid condition and areas of inflammation.

She was given 2 CVP capsules t.i.d. in addition to a special diet. After 3 days, there was less blood in the stools and after 5 days, it was found only by the guaiac test.

The patient was discharged from the hospital, markedly improved, and told to continue her diet and CVP capsules. After being home for a week, she

had recurrence of her symptoms and was again sent into another hospital where she remained for three weeks.

Jan. 26, 1955—weight 166 lbs., no diarrhea, no blood in stools. Feb. 11, 1955—X-ray showed a fairly well functioning colon. During all this time, she received CVP capsules, one after meals.

**Remarks:**—A case of bleeding ulcerative colitis treated with resion and polymyxin and CVP, responded to this combined therapy. Bleeding was arrested promptly in spite of the fact that polymyxin exerts slight hemolytic properties.

Our clinical trials cover 53 cases of gastrointestinal hemorrhage and two cases of persistent epistaxis; one case of epistaxis caused by ulceration of the nasal mucosa and the other case was that of hypertension. In both cases, bleeding was promptly stopped by administration of CVP. The 53 cases of gastrointestinal hemorrhage are summarized in the following table.

TABLE I  
EFFECT OF CVP ON GASTROINTESTINAL HEMORRHAGE

Condition	No. of cases	CVP daily dose	Results		
			Good	Satis- factory	Negative
Bleeding duodenal ulcer, gastric erosions	4	300-600 mg.	2	2	
Bleeding duodenal ulcer	12	300-600 mg.	10	2	
Duodenal ulcer cicatrized, pyloric obstruction	1	300 mg.			1
Bleeding gastric ulcer	2	600 mg.	2		
Bleeding mucous colitis	3	400-600 mg.	2	1	
Hemorrhagic ulcerative colitis	14	300-600 mg.	5	5	4
Diverticula of colon, bleeding	3	300-600 mg.	1	2	
Gastric hyperacidity with erosions	1	300 mg.		1	
Anal pruritus	1	300 mg.		1	
Hemorrhoid bleeding & rectal ulceration	7	300-600 mg.	5	2	
Anal fissure	1	300 mg.			1
Rectal bleeding carcinoma	1	300 mg.			1
Jaundice, infectious hepatitis, epistaxis	3	600 mg.	1		2

The results of our clinical investigation indicate that bleeding duodenal ulcer responded in the most satisfactory manner to the treatment with CVP. In 10 out of 12 cases of noncomplicated duodenal ulcer, the results were good and in two cases, satisfactory. In two cases of bleeding gastric ulcer, CVP arrested bleeding. The salutary effect of CVP was evidenced in some cases of ulcerative colitis (5—good; 5—satisfactory) while in 4 cases, no improvement was noticed. In rectal and hemorrhoidal bleeding, CVP was beneficial. In five cases, the response was good and two cases, satisfactory. In two cases of infectious hepatitis with jaundice and hemorrhagic diathesis, the results were negative, but in one case, complicated by hypertension, epistaxis and mild pruritus, the effect of CVP was good. In one case of acute pruritus, apparently induced by antibiotics, CVP brought relief.

#### COMMENT

In their papers, Biskind and Martin<sup>22,23</sup> and Sokoloff<sup>24</sup> revealed the anti-inflammatory properties of bio-flavonoids, a property to which they attribute the beneficial effect of these compounds upon capillary activity. The classic work of Menkin<sup>34</sup> fully demonstrated the prime role of the capillary system in localized inflammatory processes. An injury to the capillary wall unavoidably complicates and often initiates inflammation of epithelial tissue. In gastrointestinal hemorrhage, there always is a localized inflammatory state of the mucous membrane, associated with considerable injury to the capillaries and the precapillary arterioles.

The injury to the capillary wall, with a consequent inflammation of the mucosa, can be brought about by nutritional defects, neurogenic factors, bacterial and chemical toxins and other factors. This may explain the multiplicity of etiologic factors responsible for such conditions as peptic ulcer or ulcerative colitis. In this respect, the beneficial effects of bio-flavonoids in gastrointestinal hemorrhage deserve fuller attention and further investigation on the part of gastroenterologists.

The increase in the number of bleeding peptic ulcer and ulcerative colitis cases which we have all noticed in recent years, might be attributed not only to the environmental conditions in which modern man lives, with their stress and worries, but also to the use, or rather misuse, of antibiotics, many of which have an irritating and even harmful effect on the mucous membrane of the digestive tract. Certain of the new widely used steroids may also cause a flare-up of latent peptic ulcer.

The recent work of Mandelbaum, et al<sup>35</sup>, Morrow, et al<sup>36</sup>, Schroeder<sup>37</sup>, and Sieber, et al<sup>38</sup> upon the side-effect of hydralazine and hexamethonium is of particular interest. According to them, these compounds might initiate bleeding in dormant and latent peptic ulcer and other gastrointestinal conditions. The toxic effect of chloramphenicol is well-known and its disturbing effect on the

intestinal flora and mucous membrane has been reported by many authors (Harris<sup>39</sup>; Woods, et al<sup>40</sup>; Manheim<sup>41</sup>; McGovern, et al<sup>42</sup>; Smith<sup>43</sup>).

Aureomycin and terramycin, although less toxic than chloramphenicol, still have a deteriorating effect on bacterial flora according to Gewin and Friou<sup>44</sup>, Smith<sup>43</sup>, Panzion<sup>45</sup>, Welch<sup>46</sup> and others. From this point of view, the use of bio-flavonoids, because of their anti-inflammatory and capillary permeability features might be recommended as a supplement to antibiotic therapy. We found that CVP minimized the side-effects of antibiotics, a fact of prime importance when one deals with gastrointestinal hemorrhage.

#### SUMMARY

Fifty-three cases of gastrointestinal hemorrhage and two cases of persistent epistaxis were treated with CVP, citrus bio-flavonoid compound.

Two cases of epistaxis, one that of hypertension, responded promptly to this therapy.

Sixteen cases of bleeding duodenal ulcer, four of which had gastric erosions, responded favorably to CVP. In 12 cases, the results were good, in four cases, satisfactory.

Salutary effect of CVP was evidenced in two cases of bleeding gastric ulcer. In one case of duodenal cicatrized ulcer with gastric obstruction, there was no beneficial effect from CVP.

In seven cases of bleeding mucous and ulcerative colitis the results were good, in six—satisfactory and in four, negative.

In one case of diverticula of the colon, with bleeding, the response to CVP was good and in two cases, satisfactory.

The results of CVP in the treatment of rectal and hemoroidal bleeding were good in five cases, and satisfactory in two.

One case of infectious hepatitis with jaundice and epistaxis responded quite satisfactorily to CVP but in two cases of hepatitis the results were negative.

In one case of anal fissure and one case of rectal bleeding, postoperative carcinoma, there was no improvement.

The case of anal pruritus induced by antibiotics was relieved by the CVP therapy.

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## A NEW APPROACH TO THE MANAGEMENT OF PEPTIC ULCER BY INDUCING SUSTAINED GASTRIC INACTIVITY\*

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In the medical management of peptic ulcer, great emphasis has been placed on the importance of the suppression of gastric secretion and relatively minor effort has been made to allay gastric motility and pyloric activity. It is the object of this paper to evaluate the therapeutic effect on peptic ulcer resulting from inactivation of gastric peristalsis by an anticholinergic drug.

No attempt will be made to minimize the importance of the accepted standard dietary and antacid approach in the treatment of peptic ulcer. Historically, Sippy's<sup>1,2</sup> contribution has been outstanding in this regard. In addition, the important role played by various buffering, antacid and secretory inhibitor agents is well established. If, however, in addition to these beneficial effects, further improvement could be obtained by the inhibition of gastric motor activity, then a greater therapeutic efficacy would be attained.

The therapeutic value of inactivating gastric motility has been forcibly demonstrated by the surgical experience of "vagotomy" or "vagectomy" by Dragstedt and his associates<sup>3,4,5</sup> and others<sup>6,7</sup>. This procedure, however, is not only too formidable to apply to routine peptic ulcer patients but also has several disadvantages<sup>8,9</sup>.

With the advent of the anticholinergic drugs, it appeared that the dream of a "medical vagotomy" would be realized. They gave pharmaceutical promise of suppressing gastric secretion and motility. Although the literature is replete with confirmation of their secretory inhibiting efficacy, there is a relative paucity of material concerning their effect on gastric motor activity.

Recently, limited objective studies have been carried out on gastric motility. These, in a measure substantiated some clinical impressions. Asher<sup>10</sup> observed gastroscopically that methantheline bromide (Banthine) when administered intravenously, will cause cessation of gastric peristalsis. Stempien et al<sup>11</sup> have observed endoscopically, that the normal gastric mucosa varied in function from hypo- to hyperfunction. In gastric disease such as gastritis and peptic ulcer,

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however, increased gastric activity is uniformly present. Hightower et al<sup>12</sup>, using the balloon photokymographic technic, have actually correlated antral gastric hypermotility with epigastric pain. They also demonstrated that Banthine inhibited hypermotility and allayed pain. Similar findings were reported by Abbot et al<sup>13</sup>. They made direct observations on the gastric fistulous subject TOM, after introduction of Banthine 50 mg. Another contribution on the effect of anticholinergic drugs on gastric motility was made by Hawkins et al<sup>14</sup>. Using the x-ray technic, they demonstrated "marked delay in gastric emptying".

The above studies, however, were limited in scope and somewhat inconclusive. Several pertinent questions of clinical significance remained to be answered. Some of the questions concerning the gastric motor effect of the parasympathetic blocking agents were:—What degree of inhibition of motility is produced by the administration of the recommended pharmaceutical doses

TABLE I  
COMPARATIVE RESPONSE TO THERAPY

	<i>Clinic Cases</i>	
	<i>Standard method</i>	<i>Intensive anticholinergic method</i>
Duration of treatment	1 to 12 months mean 4.5 months	8 to 30 days mean 17 days
Type of response	Good in 8 cases 31% Poor in 17 cases 69%	Good in 22 cases 88% Poor in 3 cases 12%
<i>Private Cases</i>		
Duration of treatment	% to 12 months mean 2.9 months	6 to 26 days mean 14.1 days
Type of response	Good in 19 cases 76% Poor in 6 cases 24%	Good in 23 cases 92% Poor in 2 cases 8%

in humans? Is it possible to induce relative complete cessation of peristalsis? Can we cause relaxation of the pylorus? What doses are required to accomplish these phenomena? How long would such gastric inactivity last from a given dose? Finally, how would arrest of gastric motility affect the patient and would it have any therapeutic value?

The answers to some of these questions were elicited by a preliminary objective investigation<sup>15</sup>. Following the administration of progressively increasing doses of propantheline bromide (Pro-Banthine), a bromide salt of a quaternary amine, gastroscopic observations were made of its anticholinergic effect. It was demonstrated by this method that in contrast to parenteral administration, the recommended pharmaceutical oral doses had moderate or no effect on gastric motility and pyloric function. When, however, relatively larger amounts (two times the recommended dose), was used a truer parasympathetic blocking was

attained. Relative complete gastric inactivity was induced. Peristalsis stopped rather suddenly and gastric relaxation ensued. At the same time, the rhythmic opening and closing of the pylorus also ceased and left it in a relaxed state. Another contribution of this study was the demonstration that the gastric motor inactivity effect was of relatively short duration, lasting only for about one hour and ten minutes.

Once we established the fact that the attainment of gastric motor inactivity was feasible, the logical sequence was to apply this principle to the treatment of peptic ulcer. In order for us to induce sustained gastric motor inactivity, it became evident that not only did we have to give larger amounts of the anticholinergic drug but the frequency of administration had to be increased.

#### DOSAGE AND METHOD OF ADMINISTRATION

Propantheline bromide (Pro-Banthine) was used as the anticholinergic drug. Instead of the patient receiving the recommended dose of four to eight tablets, 60 to 120 mg. daily, our cases were given as much as 18-22 tablets or 270 to 330 mg. The dosage and frequency of administration was so arranged that it would not interfere with gastric emptying during meal time. The patient was instructed to start taking the medication 1½ hours after breakfast and to take two tablets (30 mg.) every 1½ hours, throughout the day except during meal time, when the time interval was lengthened. After some experimentation, the following schedule was adopted. Breakfast at 7:30 A.M., then two tablets at 8:30 A.M., 10:00 A.M., 11:30 A.M.—Lunch at 12:30, followed by two tablets at 2:00 P.M., 3:30 P.M., 5:00 P.M.—Dinner at 6:00 P.M., then two tablets at 7:30 P.M., 9:00 P.M., 10:30 P.M., and before retiring or at any time on awaking during the night. The patient was allowed to have three regular meals a day. The only restriction being that he was prohibited from using coffee, alcoholic beverages, smoking and condiments.

#### METHOD OF STUDY

Fifty patients were selected for this investigation. They were divided into two groups of 25 each. One division were indigent cases, attending a clinic in a city hospital, who were poorly controlled. The second group, acting as a control, were treated under optimum conditions, in private practice. They all had clinical as well as roentgen evidence of peptic ulcer. They were all ambulatory. Their ages ranged from 19 to 77 years.

Both groups were on standard ulcer therapy, prior to the initiation of the intensive anticholinergic treatment. The standard management consisted of an ambulatory ulcer diet (six feedings daily), antacid medication one hour p.c. and propantheline bromide (Pro-Banthine) 15 mg. q.i.d., after meals and before retiring. Although the response to standard therapy was favorable in the private group, it was poor in the clinic patient division. The results in the latter group

TABLE II  
SIDE REACTIONS OF FIFTY PATIENTS  
TAKING LARGE AMOUNTS OF PRO-BANTHINE, DAILY

Clinic patients									
No.	Patient	Age	Sex	Dose. No. of tablets taken in 24 hrs.	Xerostomia	Cycloplegia	Bladder atony	Constipation	Tachycardia
1.	M.R.	20	F	18-20	++	+	0	0	0
2.	J.P.	32	M	18-20	++	0	0	0	0
3.	F.M.	52	F	18-20	++	0	0	0	0
4.	J.F.	40	M	18-20	++	0	0	+	0
5.	A.D.	31	F	18-20 Reduced to 10	++	+	+	+	0
6.	S.N.	58	M	18-20	+++	0	0	+	0
7.	M.S.	62	F	20	++	0	0	0	0
8.	S.E.	53	F	20	++	0	0	0	0
9.	E.L.	19	M	20	++	0	0	0	0
10.	L.S.	57	M	20	++	+	0	0	0
11.	S.M.	42	F	20	++	0	0	0	0
12.	N.S.	36	M	20	+	0	0	0	0
13.	W.B.	40	M	20	++	0	0	0	0
14.	F.H.	28	F	18	+	0	0	0	0
15.	G.S.	66	M	20	++	0	0	0	0
16.	J.M.	50	M	20	++	0	0	0	0
17.	W.H.	54	M	20	++	0	0	0	0
18.	W.H.	53	M	22	++	0	+	0	0
19.	R.D.	77	M	20	+	0	+	0	0
20.	G.C.	38	F	20-30 Daily	++	0	+	0	0
21.	S.B.	40	F	18-20	+++	0	0	0	0
22.	Y.S.	30	M	18	+++	0	0	0	0
23.	A.K.	53	M	18-20	++	0	+	0	0
24.	M.P.	62	F	18-20	++	0	0	0	0
25.	A.G.	40	F	18	++	0	0	0	0

TABLE II (*continued*)*Private patients*

No.	Patient	Age	Sex	Dose. No. of tablets taken in 24 hrs.	Xerostomia	Cycloplegia	Bladder atony	Constipation	Tachycardia
1.	M.A.	45	F	20	+	0	0	0	0
2.	L.C.	66	M	20	++	0	+	0	0
3.	F.L.	78	F	18	+	0	0	0	0
4.	W.S.	38	M	20	+	0	0	0	0
5.	E.S.	73	M	16	+	0	0	0	0
6.	E.S.	51	F	20	++	0	0	+	0
7.	B.S.	43	M	18	+	0	0	0	0
8.	M.S.	34	M	20	+	0	0	0	0
9.	L.R.	18	M	20	++	0	0	0	0
10.	J.Mc.	26	M	20	+	0	0	0	0
11.	S.M.	66	M	18	++	0	+	0	0
12.	M.P.	69	F	20	+	0	0	0	0
13.	M.P.	36	F	20	++	0	0	0	0
14.	L.P.	29	M	20	++	0	0	0	0
15.	R.P.	57	F	16-20	+	0	0	0	+
16.	M.H.	46	F	20	+	0	0	0	0
17.	A.H.	74	M	14-18	+	0	0	0	0
18.	M.H.	53	M	20	++	0	0	0	0
19.	R.H.	53	F	20	+	0	0	0	0
20.	E.F.	44	M	20	+	0	0	0	0
21.	F.F.	37	M	20	+	0	0	0	0
22.	B.K.	31	F	20	++	0	0	0	0
23.	H.C.	47	F	20	+	0	0	+	0
24.	D.W.	65	M	16-20	++	0	0	0	0
25.	J.F.	48	F	20	+	0	0	0	0

were discouraging for several reasons. The majority of our indigent patients had language difficulty and did not understand the nurses' instructions. Some did not want to follow the required regimen. Others lacked the means with which to purchase their dietary requirements. In addition, social service studies of these individuals indicated serious environmental stress factors. It is evident that under the circumstances, we were faced with a rigid test for our new approach to the problem. Both groups were placed on the intensive anticholinergic treatment and a comparative evaluation of their response to it and the standard therapy was made.

TABLE III  
SUMMARY OF  
AN EVALUATION OF SIDE REACTIONS IN FIFTY PATIENTS  
TAKING 18-22 TABLETS (270-330 mg.) OF PRO-BANTHINE DAILY

Side-effects	Degree of reaction		
	Marked	Moderate	None
Xerostomia	3	47	0
Cycloplegia	0	3	47
Bladder atony	0	9	41
Constipation	0	3	47
Tachycardia	0	1	49
Blood pressure	0	0	50

#### RESULTS OF THERAPY

The results of treatment were evaluated both clinically and roentgenographically. The clinical response was based on the degree of relief from symptoms and the x-ray response was measured by the demonstration of the healing of the ulcer. The efficacy of therapy was designated as good when it was substantiated by both clinical and roentgen evidence. It was recorded as poor when either one or both failed to show improvement.

Our clinic patients' response to the standard ulcer therapy was unfavorable, even though they were treated from 1 to 12 months with a mean of 4.5 months by this method. Eight patients or 31 per cent showed a good effect and 17 or 69 per cent obtained poor results. In sharp contrast, when the same indi-

viduals were placed on the intensive anticholinergic treatment, the duration of therapy lasted 8 to 30 days, with a mean of only 17 days. The response was good in 22 patients or 88 per cent and poor in the remaining three or 12 per cent. Our good results with this new approach to our difficult cases was beyond our expectations. Not only was the mean duration of treatment reduced from 135 to 17 days, but more astonishing, the incidence of good response jumped from 31 to 88 per cent. Another interesting aspect of this study is that two duodenal ulcer cases (Nos. 4 and 18), with a five-hour gastric retention of 60 and 25 per cent respectively, were among our good results. Without resort to gastric lavage or hospitalization, their symptoms subsided, they gained weight and showed roentgen evidence of normal gastric emptying after a three-week period.

Although our private patients did much better than the clinic cases with the standard method of management, they too showed still more favorable results with the intensive anticholinergic method. The history in this group indicated that the duration of treatment with standard therapy in the past was from one-half to 12 months with a mean of 2.9 months. The response was good in 19 cases or 76 per cent and poor in six or 24 per cent. In contrast, there was a marked reduction of time the patient was treated with the intensive anticholinergic method. It varied from only 6 to 26 days, with a mean of 14.1 days. In addition, good results rose to 23 cases or 92 per cent and poor responses were reduced to two individuals or 8 per cent.

A total of five individuals failed to respond to the intensive anticholinergic treatment. Three were in the clinic group. One case (No. 6), was a male, aged 66, who had a prepyloric ulcer with associated "narrowing and irregularity of the antrum". Malignancy was suspected. The second patient (No. 19), was a male, aged 77. He did not return after a two-week period of treatment. During this time of observation, he improved only slightly. The third patient (No. 25), was a female, aged 40, with a duodenal ulcer where "penetration" was suspected. The cause of failure in the private case (No. 3), a female, aged 78, was due to the presence of a fixed pyloric obstruction which may have been due to an advanced scarred ulcer or possibly to carcinoma. She showed signs of marked malnutrition and suffered from coronary artery diseases which finally caused her demise. The second failure occurred in case (No. 8), a male postal employee, aged 34, who had multiple psychogenic problems, with irregular hours of eating and sleeping and was an extremely heavy smoker.

#### SIDE REACTIONS

In using such large unconventional amounts of the anticholinergic drug, caution was exercised. In our early cases, the dose as well as the frequency of administration was gradually increased. Careful observations of our patients for toxic effects and side reactions were made. In the study of our 50 cases,

such side-effects as xerostomia, cycloplegia, bladder atony, constipation, tachycardia and effect on blood pressure were evaluated (Tables II and III).

It was surprising as well as gratifying to us, how relatively well such large doses of propantheline bromide (Pro-Banthine), were tolerated. Few anticipated side reactions materialized. Xerostomia, was by far, the most troublesome complaint. All of our patients experienced a varying degree of dryness of their mouth. In three, it was marked and caused discomfort. In all instances, however, xerostomia diminished in intensity after a few days. Only three patients had a moderate disturbance in accommodation on reading. Some bladder atony was encountered in nine individuals. This was not a direct complaint, but was rather elicited by questioning the patient. In all instances, it was relatively mild. They experienced a moderate urinary hesitancy. This disturbance disappeared after two to four days while on the medication. Only three cases developed mild constipation during the treatment. Certainly, less than would be anticipated from a bland smooth diet. Apparently, even large amounts of the drug does not affect colonic motility. Only one of our patients developed a mild tachycardia. Another side-effect which was studied was anhydrosis. This was difficult to evaluate clinically. Most of our cases could not give a reliable description of the comparative amount of sweating, while on or off the medication. A study of the effect on blood pressure was also made and no important changes were observed. Finally, no significant gastric retention, demonstrable by x-ray, was encountered when the administration of the medication was spaced, according to the indicated schedule of 2½ hours apart during meal time.

#### COMMENTS

Thomas<sup>16</sup> has expressed the point of view, that in theory, "therapy with a good anticholinergic drug should be more effective than vagotomy. Whereas vagotomy merely disconnects the enteric plexuses from the central nervous system, leaving the peripheral reflex mechanism structurally intact, these drugs act to depress the most peripheral parasympathetic nerve endings, thus nullifying the effect even of the local reflexes." In addition, most of the anticholinergic agents possess some degree of "ganglionic blockade". "This latter action is exerted on sympathetic as well as parasympathetic ganglia".

Our successful results tend to prove that these theoretical considerations can be attained clinically by increasing the dosage and the frequency of administration of propantheline bromide (Pro-Banthine). Sustained gastric inactivity can be induced. Not only is gastric secretion suppressed<sup>17,18</sup>, but peristalsis is inhibited and the pylorus is relaxed. The dream of a controlled "medical vagotomy" is now nearer realization. With this method, the clinician can virtually, at will, turn on and off his "vagotomy".

Apparently, the rate of excretion or destruction of propantheline bromide (Pro-Banthine), is rapid for no evident cumulative toxic effects or serious side

reactions were observed from the administration of large daily amounts of the drug. Although xerostomia was the most common complaint, our patients adjusted themselves to it. The anticipated hazard of urinary retention experienced with similar drugs, did not materialize. When bladder atony did occur, it was relatively mild and transient. Caution, however, should be exercised in the management of the elderly male patient as our experience at this time is too limited to be conclusive. Another interesting finding was that constipation did not develop in the majority of instances. Blurring of vision, tachycardia or evidence of any other side reactions were negligible. Apparently, not all the anticholinergic drugs have similar widespread action. There seems to be some selectivity in the degree of response by organs innervated by the parasympathetic system to different anticholinergic agents.

Whereas, more extensive side-effects have been encountered with relatively smaller amounts of other drugs<sup>19,20,21</sup>, fewer patients experienced relatively innocuous side reactions with massive doses of propantheline bromide (Pro-Banthine). It is evident that each anticholinergic drug should be evaluated on its own clinical merits, rather than on generalizations.

The subsidence of pain, although most dramatic to the patient, should not be taken as a measure of the healing of the ulcer, for many of our patients experienced this relief within a matter of hours. Reliance must be placed on roentgen demonstration of adequate healing of the ulcer.

#### SUMMARY

It has been demonstrated gastroscopically, that gastric motor inactivity can be attained by increased doses of propantheline bromide (Pro-Banthine). In order to induce sustained inhibition of gastric motility, not only did we have to increase the dose of the anticholinergic drug, but the frequency of administration also had to be increased.

Application of this principle to the management of peptic ulcer resulted in unusual successful therapeutic responses. A clinic group of patients, difficult to manage, responded poorly to standard treatment. In sharp contrast, when placed on the intensive anticholinergic form of therapy, they did remarkably well. The incidence of good results rose from 31 to 88 per cent and the mean duration of therapy decreased from 4.5 months to 17 days. A control group, treated privately under optimum conditions, although doing well under standard treatment, also showed still more favorable results with the intensive anticholinergic method. The incidence of good responses increased from 76 to 92 per cent and the mean duration of management decreased from 2.9 months to 14.1 days.

No serious toxic effects or side reactions were observed as the result of the use of such large unconventional amounts of the drug.

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## GASTRIC ANALYSIS WITHOUT INTUBATION\*

### SURVEY AND EVALUATION OF THE TUBELESS (DIAGNEX) METHOD FOR DETERMINATION OF FREE HYDROCHLORIC ACID

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In a recent editorial, Weiss<sup>1</sup> made the following statement with regard to the subject of gastric analysis. "The old method of analyzing the fasting gastric content or the use of the Ewald or Boas Test meal extracted by means of a stomach or duodenal tube, may now be relegated to the past." He was referring to the new tubeless method of gastric analysis. Attempts to find a tubeless method for the determination of achlorhydria have been made in the past. Included amongst them was the "combined test" for gastric acidity reported by Matzner and associates<sup>2</sup> which was based on the postprandial change in urinary reaction as an index of gastric acidity. Their report indicated an alkaline tide in individuals having a normal gastric acidity, with a relative fixation of the urinary pH in those exhibiting a true achlorhydria.

This tubeless method, based upon the use of a quinine exchange resin for the determination of the presence or absence of free hydrochloric acid, was first introduced in 1950 by Segal and his associates<sup>3</sup>. Subsequent reports by the same group of investigators<sup>4-6</sup> further emphasized the degree of accuracy and information obtained from this test. Many additional favorable reports have appeared in subsequent publications. A recent independent survey of 90 cases was reported by Becker and Maslon<sup>7</sup>.

The indications for gastric analysis with special emphasis on the significance of achlorhydria, has been well established. The frequent relationship of an acidity or achlorhydria with gastric cancer has been reported since 1879 by von den Velden<sup>8</sup>. Statistics and investigations have continually been reported, endeavoring to enhance the problem of early diagnosis of gastric cancer. An extensive study of the possible predisposition to gastric cancer by State<sup>9</sup> and his group again emphasized the frequent association of achlorhydria with gastric cancer. Cancer detection by screening gastrointestinal patients or the general population for achlorhydria has been suggested. This group with known achlorhydria, with or without gastrointestinal symptoms, should be subjected to further methods of investigation in an attempt to obtain earlier diagnosis of gastric cancer. It is apparent that this may lead to more effective surgical therapy.

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TABLE I  
DETECTION OF ACHLORHYDRIA CASES

Absence of free gastric hydrochloric acid (in 2-hour Urine excretion). Oral ingestion of 2 gm. of Quininium Cation resin.

Case	Diagnosis	Gastric acidity Intubation method			(Diagnex)			
		F—Fasting	H—Histamine stimulant	T—Topfers Reagent	Quininium Cation in Urine Comparison Fluorescence with Standards.	C—Control	1—1st hour collection	2—2nd hour collection
		F	H	T				3—Sum of first 2 hours
1—M/55	Unestablished	0	0	0	0	0	0	0
2—F/61	Unestablished	0	0	0	0	0	0	0
3—M/57	Chronic Gastritis	0	0	0	0	0	0	0
Repeat	Chronic Gastritis	0	0	0	0	5	5	10
Repeat	Chronic Gastritis	0	0	0	0	0	0	0
4—M/60	Carcinoma	0	0	0	0	5	5	10
5—M/71	Pernicious Anemia	0	0	0	0	10	5	15
6—F/59	Pernicious Anemia	0	0	0	0	0	0	0
7—M/61	Carcinoma (Lymphosarcoma)	0	0	0	0	0	0	0
8—F/60	Pernicious Anemia	0	0	0	0	0	0	0
Repeat	Pernicious Anemia	0	0	0	0	0	0	0
9—M/50	Carcinoma	0	0	0	0	0	5	5
10—M/31	Gastritis	0	0	0	0	5	10	15
11—M/58	Gastritis	0	0	0	0	5	5	10
12—M/79	Carcinoma Pernicious Anemia	0	0	0	0	0	0	0
13—M/64	Unestablished	0	0	0	0	0	5	5
14—M/64	Postsplenectomy	0	0	0	0	0	5	5
15—M/59	Chronic Gastritis	0	0	0	0	0	0	0
16—M/45	Chronic Gastritis	0	0	0	0	5	5	10
17—M/44	Unestablished	0	0	0	0	0	5	5
18—M/49	Postulcer Gastrectomy	0	0	0	0	0	15	15
19—M/55	Unestablished	0	0	0	0	0	5	5
20—M/59	Gastric Polyp	0	0	0	0	0	10	10

TABLE I (*continued*)

Case	Diagnosis	Gastric acidity Intubation method F—Fasting H—Histamine stimulant T—Topfers Reagent			(Diagnex) Quininium Cation in Urine Comparison Fluorescence with Standards. C—Control 1—1st hour collection 2—2nd hour collection 3—Sum of first 2 hours			
		F	H	T	C	1	2	3
21-M/42	Chronic Gastritis	0	0	0	0	0	5	5
Repeat	Chronic Gastritis	0	0	0	0	0	10	10
Repeat	Chronic Gastritis	4u	8u	0	0	5	15	20
22-M/57	Unestablished	0	0	0	0	5	5	10
23-M/48	Gastric Polyp	0	0	0	0	0	0	0
24-F/41	Unestablished	0	0	0	0	0	0	0
25-M/48	Unestablished	0	0	0	0	0	5	5
26-M/45	Unestablished	0	0	0	0		5	5
27-F/59	Chronic Gastritis	0	0	0	0	5	5	10
28-M/57	Chronic Duodenal Ulceration—Gastritis	0	0	0	0		10	10
29-M/55	Chronic Gastritis	0	0	0	0		5	5
30-M/76	Hiatus Hernia Hypertension	0	0	0	0	0		0
31-M/61	Gastritis	0	0	0	0	0	0	0
32-M/55	Gastritis	0	0	0	0	0	5	5

The rationale of this tubeless method of gastric analysis is based on the knowledge of ion exchange resins<sup>10</sup>. Diagnex\* is an indicator cation exchange compound, containing 20-28 mg. of quinine as the indicator cation per gram of Amberlite XE-96 as the carboxylic cation exchange resin<sup>11</sup>. The method involves the release of quinine cation from the synthetic ion exchange resin by the hydrogen ion in the gastric secretion. When free hydrochloric acid is present in the stomach, the quinine thus released is absorbed from the small intestine. Quinine will appear in the urine excreted within two hours after the administration of the resin compound. When no free gastric hydrochloric acid is present in the stomach, the quinine of the indicator resin is not displaced and none will appear in the excreted urine samples taken for a period of two hours.

\*Diagnex—Supplied by E. R. Squibb & Sons.

The urine assay for quinine is carried out on the specimens submitted by the modification of the Kelsey-Geiling<sup>12</sup> technic. This simplified procedure is as follows:

1. Dilute entire quantity of urine sample to 300 c.c. with distilled water.
2. Alkalize 30 c.c. of this dilution with 5 c.c. of half-normal sodium hydroxide.
3. Add 15 c.c. of ether—shake gently. Allow to stand for separation of layers, adding a few drops of 95 per cent ethyl alcohol to achieve sharpness.
4. 8.2 c.c. of the upper ether layer is extracted with 5 c.c. of 0.1N sulphuric acid. Shake gently to obtain clear layers.
5. 5 c.c. of the sulphuric acid extract is collected for quinine determination by fluorescent light.

A special Diagnex Assay Separatory funnel<sup>\*</sup> was used routinely on all urine samples submitted. The simplicity and convenience of using this apparatus was very apparent. Fluorescent examination, comparison and interpretation of urinary quinine is obtained in the following manner. In this series, the 4-Watt Ultraviolet Lamp† was used. This can be housed for daylight use. Other means of ultraviolet irradiation can be used. The Diagnator‡ an optical fluorescence comparator is now being used for more accurate and semiquantitative comparison with standards of urinary quinine. More accurate means of determinations require the use of a photofluorometer. As will be shown later, the semi-quantitative analysis and interpretation is adequate for free hydrochloric acid detection.

Standard quinine solutions used for comparison in this survey, were prepared from tablets of quinine hydrochloride equivalent to 1.5 mcgm. of quinine base. Separate dilutions with 0.1N sulphuric acid in six test tubes are made giving figures at 5 to 30 mcgm. of quinine in urine equivalent to 0.25 to 1.5 mcgm. of quinine in the standard. Of interest, several series of standards so prepared were wax cork stoppered and stored in a refrigerator. They were repeatedly compared to freshly prepared standards and found to be stable for a period of six months.

Segal<sup>6</sup> has previously reported that more than 25 mcgm. of quinine was indicative of the presence of free hydrochloric acid.

The purpose of the present survey and report is to evaluate gastric analysis with the tubeless technic herein described, and its comparison with conven-

\*Mfg. Will Corp., N.Y.C.

†Blak-Ray Lamp Model X4-so. Pasadena, Calif.

‡Photovolt Fluorescent Comparator Mod. 60, N.Y.C.

TABLE II  
DETECTION OF POSITIVE CASES (Free HCl Present)

Case	Diagnosis	Intubation			Diagnex				
		F—Fasting Free HCl	H—Posthistamine T—Topfers Reagent	C—Control	1—1 Hour Urine	2—2 Hour Urine	3—Total of 1 plus 2 hr.	CB—Combined 2 hr. recovery	
		F	H	H	C	1	2	3	CB
1—F/54	Unestablished	20	52	+	0	25	20	45	
2—F/56	Unestablished	15	45	+	0	25	25	50	
3—F/59	Diverticulum Esophagus Atrophic Gastritis	14	35	+	0	15	25	40	
4—M/49	Duodenal ulcer	0	100	—	0	0	30	30	
Repeat	Duodenal ulcer	35	65	+	0	15	20	35	
5—M/54	Duodenal ulcer Chronic pyloric obstruction gastrectomy performed	0	0	—	0	25	25	50	
Repeat	Duodenal ulcer Chronic pyloric obstruction gastrectomy performed	10	20	+	0	20	30	50	
6—F/52	Secondary anemia	15	15	+	0	5	20	25	
7—F/56	Unestablished	10	20	+	0	0	30	30	
8—F/56	Anemia	15	20	+	0	5	25	30	
9—M/52	Duodenal Ulcer	25	50	+	0	5	15	20	
10—F/55	Chronic Colitis	10	30	+	0	30	30	60	
11—F/60	Anemia	15	45	+	0	30	30	60	
12—F/49	Duodenal Ulcer	15	40	+	0	10	30	40	
13—M/69	Gastrectomy 20 yrs. Duodenal Ulcer	15	35	+	0	5	20	25	
14—M/58	Gastric Neurosis	0	0	—	0	30	30	60	
Repeat	Gastric Neurosis	15	45	+	0	25	30	55	
15—F/36	Colitis Syndrome	15	40	+	0	20	30	50	50
16—F/48	Plummer-Vinson (Globus)	10	25	+	0	15	15	30	
17—F/44	Unestablished	20	35	+	0	20	20	40	40
18—M/59	Peptic ulcer Syndrome	25	65	+	0	5	20	25	25
19—M/51	Unestablished	15	35	+	0	5	20	25	25

TABLE II (*continued*)

Case	Diagnosis	Intubation F—Fasting Free HCl H—Posthistamine T—Topfers Reagent			Diagnex C—Control 1—1 Hour Urine 2—2 Hour Urine 3—Total of 1 plus 2 hr. CB—Combined 2 hr. recovery				
		F	H	H	C	1	2	3	CB
20-M/42	Peptic Ulcer Syndrome	20	60	+	0	15	30	45	50
21-M/63	Ulcer Syndrome	30	75	+	0	10	15	25	
22-F/50	Unestablished	15	30	+	0	15	30	45	50
23-F/60	Unestablished	20	40	+	0	20	20	40	40
24-M/55	Chronic Duodenal ulcer	40	90	+	0	15	20	35	40
25-M/62	Chronic Duodenal Cholecystitis	10	15	+	0	10	25	35	40
26-M/72	Chronic Duodenal ulcer	30	65	+	0	20	30	50	50
27-F/48	Chronic Duodenal Ulcer	40	90	+	0	15	30	45	50
28-M/58	Gastrectomy Cholejejunostomy Pancreatitis	20	70	+	0	15	30	45	50
29-M/48	Sprue—Non Tropical	20	40	+	0	20	25	45	50
30-M/61	Hematemesis	25	65	+	0	20	30	50	50
31-M/45	Gastritis	30	70	+	0	5	20	25	25
32-F/56	Unestablished	10	20	+	0	20	20	40	50
33-M/48	Duodenal Ulcer	30	55	+	0	15	25	40	40
34-M/51	Chronic Duodenal Ulcer	20	70	+	0	20	30	50	50
35-F/58	Chronic Pneumoperitoneum probable ulcer Fistulae	15	35	+	0	15	15	30	30
36-M/53	Duodenal Ulcer	20	55	+	0	10	20	30	30
37-M/51	Chronic Duodenal ulcer	15	66	+	0	15	30	45	50
38-M/47	Duodenal Ulcer	20	70	+	0	15	25	40	40
39-F/31	Neurosis	30	40	+	0	20	30	50	50
40-F/59	Possible Gastric Carcinoma	15	20	+	0		40		
41-F/60	Chronic Duodenal Ulcer	25	35	+	0	2hr		25	
42-M/52	Chronic Duodenal Ulcer	30	65	+		2hr		25	
43-M/58	Unestablished	20	40	+	0	2hr		25	
44-F/30	Chronic Duodenal Ulcer	30	40	+	0	2hr		40	

TABLE II (*continued*)

Case	Diagnosis	Intubation			Diagnex				
		F—Fasting Free HCl	H—Posthistamine	T—Topfers Reagent	C—Control	1—1 Hour Urine	2—2 Hour Urine	3—Total of 1 plus 2 hr.	CB—Combined 2 hr. recovery
		F	H	H	C	1	2	3	CB
45—M/57	Chronic Duodenal Ulcer	30	50	+	0	2hr		30	
46—F/40	Gastric Neurosis	10	20	+	0	2hr		30	
47—M/58	Unestablished	15	50	+	0	2hr		30	
48—M/52	Chronic Duodenal ulcer	15	45	+	0	2hr		25	
49—M/55	Unestablished	20	35	+	0	30			30
50—F/49	Unestablished	10	20	+	0	30			30
51—M/53	Perforated Ulcer	20	60	+	0	50			50
52—F/40	Diverticulum Esophagus	20	55	+	0	30			30
53—M/57	Peptic Ulcer	30	80	+	0	30			30
54—F/59	Duodenal Ulcer	15	25		0	30			30
55—F/66	Pulmonary TBC	5	5	±	0	30			30
Repeat	Pulmonary TBC	15	50	+	0	10	35	45	
56—M/56	Duodenal Ulcer	30	65	+	0	30			30
57—F/61	Unestablished	25	45	+	0	30			30
58—M/45	Gastric Ulcer	30	70	+	0	45			45
59—F/52	Unestablished			+	0	30			30
60—M/68	Cardiac Decompensation			+	0	40			40
61—M/44	Hyperinsulinism			+	0	40			40
62—M/49	Hiatus Hernia			+	0	40			40
63—F/45	Unestablished			+	0	40			40
64—M/51	Unestablished			+	0	40			40
65—M/70	Unestablished			+	0	60			60
66—F/58	Unestablished			+	0	30			30
67—F/52	Unestablished			+	0	30			30
68—M/54	Unestablished			+	0	30			30
69—M/63	Unestablished			+	0	50			50
70—F/63	Unestablished			+	0	50			50

tional intubation in the same patient. Modification of previous technics to enhance the procedure are noted.

The patients selected for this study were mainly from the gastroenterology clinic. As the study progressed, in-patients and patients from other clinics, were included and subjected to the same technic of testing.

Below is listed a facsimile of instruction sheet for patient participation.

- a. Date of Test .....
  - b. No breakfast
  - c. Stop all other medicine and vitamins for one day before test day.
  - d. Urinate on arising.
  - e. Save this urine for control.
1. Open CAPSULE A\* at ..... o'clock and dissolve in  $\frac{1}{2}$  glass water. Fill glass again with  $\frac{1}{2}$  glass water and drink.
    - 1a. 1 hour later urinate, then discard.
  2. Take packet of Granules B† at ..... o'clock, mixed in  $\frac{1}{2}$  glass water. (The granules do not dissolve. DO NOT chew them.) Fill glass again with  $\frac{1}{2}$  glass water and drink.
  3. Two hours later at ..... o'clock urinate and save this urine. Label and bring to clinic.

\*Caffeine Sodium Benzoate 250 mg. or 500 mg.

†Quinine Resin 2 gm.

An afternoon clinic appointment was given on the same day. Omission of lunch was required. Intubation and histamine gastric stimulation was routinely employed. Immediate determination of free hydrochloric acid in the gastric extractions was made by adding a few drops of freshly prepared Topfer's reagent. The extractions were then submitted to the clinic laboratory for quantitative titration control. The one and two hour urine samples were taken by one of us for quantitative assay.

#### RESULTS

Achlorhydria was detected in 32 individuals. Intubation in this group (Table I) failed to reveal free hydrochloric acid after histamine stimulation. Diagnex determination confirmed these intubation results in all but one case. This case, No. 21 after a third gastric analysis disclosed a finding of fasting 4 units, histamine stimulated 8 units. This established that a low acid secretor may have a negative Diagnex test.

The results of the urine used as a control are recorded in Table I. It is interesting to note that at no time was a false positive control obtained. The findings of the 1st and 2nd hour determinations are listed, plus a fourth column indicating the results of the combined 2 hour samples. This sum was always that of the 1 plus 2 hour figures. These findings suggest that for further modification and simplification, the control and 1st hour urine may be omitted. A simple determination of the one two hour urine sample appears to be adequate for this test.

In 70 cases tabulated in Table II, there was positive detection of gastric hydrochloric acid by the Diagnex Method. This was confirmed by subsequent intubation. Four discrepancies were found in this group. In these instances the Diagnex test was markedly positive. The explanation for these discrepancies appear to be, in Case 4, unstable Topfers reagent, in Case 5, gastrectomy with too rapid emptying, Case 14, an incompletely intubation related to inability of the patient to maintain the tube *in situ* for 60 minutes, and in Case 55, improper intubation with probable duodenal contents extracted. Repeated intubation of these four cases were reported positive.

The first attempts to correlate the degree of free hydrochloric acid found on intubation with amount of quinine excreted in the urine, indicated poor to no direct quantitative relationship. Low acid secretors were infrequently found. This group when found, however, gave the most difficulty. High acid secretors gave frank positive results ranging from 25 or more. Photoelectric determinations were not made in any of these cases. Gross fluorescence in a dark room was the method employed. Later studies were made with the use of the Diagnator apparatus.

#### SUMMARY AND CONCLUSION

This report describes the use of Diagnex (Quinine carbacrylic resin, type of indicator exchange compound) as a diagnostic tubeless method for detection of gastric achlorhydria. One hundred and two cases are reported using simultaneous intubation and the tubeless technic, with the results indicating a high degree of agreement between the two methods. A qualitative relationship was demonstrated. Quantitative estimations of free hydrochloric acid by this method are not reliable. Modifications requiring one two-hour urine sample is shown to be adequate, for simplification of patient participation and lessening of laboratory time without alterations of its value as a diagnostic tool. The standard quinine solutions used for comparison in this survey were found to be stable over a period of six months when adequately refrigerated and protected from exposure to light. No contraindications for routine use of this method was noted. No discomfort or side-effects from quinine or caffeine indigestion was observed. The inability to detect other contents of the stomach, as blood, lactic acid, Boas Oppler B. or exfoliative cells for cytologic studies are apparent. It is clear that intubation would be required to obtain the above information.

This test can be applied to clinical diagnosis as a screening technic and is highly recommended for routine use to detect achlorhydria.

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## EVALUATION OF CLINICAL METHODS IN GASTROINTESTINAL DISEASE\*

### VIII. PRESENT DAY THERAPY OF GASTRIC ULCER

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Peptic ulcer is a benign, nonspecific ulcer located in those portions of the alimentary tract bathed by gastric juice, such as the lower end of the esophagus, stomach, duodenum, jejunum, Meckel's diverticulum and the gastrojejunostomy (marginal) area. Some authors maintain that gastric and duodenal ulcers are different clinical entities because of the variance in the acidity, frequency of occurrence, and the greater tendency of malignancy found in gastric ulcers<sup>1</sup>.

TABLE I

PATIENTS WITH BENIGN GASTRIC ULCER STUDIED FROM AUTOPSIED AND SURGICAL SPECIMENS—AS TO NUMBER, SEX AND AGE

	Number of Patients	Percentage	Age	Number of Patients	Percentage
Autopsies	38	53	20-29	1	1.5
Surgical Specimens	34	47	30-39	7	10.
			40-49	12	17.
Total Patients	72	100	50-59	17	24.
			60-69	26	35.
Sex			70-79	8	11.
Males	53	74	80-89	1	1.5
Females	19	26	Total Patients	72	100.
Total Patients	72	100			

In a previous study of 62 autopsy cases of peptic ulcer (gastric and duodenal), the authors found 22 with lesions located in the stomach (14 along the lesser curvature, 7 near the cardia, and 1 at the greater curvature). Many of the ulcers were found in connection with other diseases such as malignancy, leukemia, arteriosclerosis, cirrhosis, chronic passive congestion of the liver, etc. Some have been cases of postoperative gastric surgery for bleeding, perforation, or penetrating ulcers. In quite a few cases the gastric ulcer was discovered at

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postmortem as an incidental finding. This relatively large number of non-malignant gastric ulcers in patients of such advanced age (average 63 years) was of interest and bespoke for the benignity of gastric ulcer at times<sup>2</sup>.

The two most controversial points regarding the treatment of gastric ulcer still revolve about the question whether medical or surgical therapy is best and whether all ulcers of the stomach should be considered potentially malignant. The present study was further pursued to evaluate the frequency of benign gastric ulcer and its conservative medical pursuit.

#### MATERIAL STUDIED

All postmortem cases with the pathological diagnosis of gastric ulcer encountered at Beth Israel Hospital (New York City), from 1931 to 1952 inclusive were examined (38 cases) as well as all surgical specimens diagnosed gastric ulcers over the same period (34 cases). These 72 postmortem and surgi-

TABLE II

**CLINICAL DIAGNOSIS IN PATIENTS WITH BENIGN GASTRIC ULCER  
CORROBORATED BY AUTOPSY AND SURGERY**

Clinical Diagnosis	Number of Patients	Percentage
No Gastrointestinal Complaints (Incidental Autopsy Finding)	19	26
Carcinoma of Stomach	15	21
Peptic Ulcer (Gastric or Duodenal)	27	37
Extragastric diagnosis (Gallbladder, Liver, Colon)	11	16
Total Number of Patients	72	100

cal specimens comprise the present study. Laboratory data such as peripheral blood counts, fecal occult blood, and gastric analyses, were performed. Repeat tests after histamine injection were performed when achlorhydria was encountered. It will be noted that such results were absent in the postmortem examinations since the gastric ulcers were incidental findings in most of the patients.

#### RESULTS

The 72 patients represented 38 (53 per cent) autopsies and 34 (47 per cent) surgical specimens. The male sex predominated. The total was 53 males (74 per cent) and 19 females (26 per cent). The most frequent age group was 50-70 years (Table I).

## CLINICAL DIAGNOSIS

The clinical history may not be of aid for differentiation as noted that the ulcer was found incidentally in 26 per cent of the autopsy cases and only 27 patients (37 per cent) presented a definite history suggestive of peptic ulcer. Some of the operated patients were considered to have malignancy by the history, but pathological examination revealed a benign gastric ulcer (21 per cent). Extragastric complaints referable to the gallbladder, liver or colon regions were encountered in 16 per cent of the patients (Table II).

## SUGGESTED HISTORY OF PEPTIC ULCER

The critical status of five patients on admission to the hospital precluded that an adequate history could be obtained. Practically ½ of the patients revealed

TABLE III  
MEDICAL HISTORY INCLUDING DURATION OF SYMPTOMS  
IN PATIENTS WITH BENIGN GASTRIC ULCER

History	Number of Patients	Percentage
No adequate history obtainable because of critical status	5	
Of remaining 67 cases:		
No history of ulcer or suggestive G.I. complaints	21	31
History of ulcer of less than 1 year duration	4	6
History of ulcer of 1-5 years' duration	20	30
History of ulcer of more than 5 years' duration	22	33
Bleeding ulcers (eroded artery noted pathologically)	11	17
Perforating or perforated ulcers	6	9.2

no gastrointestinal complaints. Eleven patients (17 per cent) entered because of a bleeding ulcer and six patients (9 per cent) because of perforation. Very few patients (6 per cent) had the ulcer less than 1 year in duration. The ulcer had been present for some time as noted by the history of complaints in 30 per cent of the patients less than five years in duration; and 33 per cent of more than five years; making a total of 63 per cent from one to more than five years' duration (Table III). This long time interval of complaints for gastric ulcer patients under conservative peptic ulcer treatment further corroborates our opinion as well as recent observers<sup>3</sup> that not all gastric ulcers are malignant.

## LOCATION OF BENIGN GASTRIC ULCERS

*Greater gastric curvature:*—As noted by others<sup>4,5</sup> gastric ulcer occurs mostly on the lesser curvature (64 per cent) and above the pylorus (18 per cent).

Three patients exhibited a gastric ulcer on the greater curvature. One was encountered at postmortem and two at operation (Table IV). Clinical diagnosis confirmed at autopsy (A-11-45) of carcinoma of the gallbladder with metastasis was made in a male patient age 51. Two deep ulcers of the greater curvature were exhibited in the absence of an ulcer history. The other two patients were operated because of a clinical diagnosis of malignancy. One patient male, age 41, presented a five-week history of epigastric pain after meals. The surgical specimen (#65981-51) revealed an elliptical ulcer penetrating along the greater curvature. These pathological surgical examinations do not corroborate the dictum of some observers that all gastric ulcers of the greater curvature are malignant and require immediate surgery<sup>6</sup>. Benign greater curvature ulcers are

TABLE IV

LOCATION, FREQUENCY AND PERCENTAGE OF BENIGN GASTRIC ULCERS  
ENCOUNTERED AT POSTMORTEM AND SURGERY

Location	Number of patients	Percentage
Lesser Curvature	46	64
Above Pylorus	13	18
Near Cardia	5	7
Posterior Wall	5	7
Greater Curvature	3	4
(In cases marked "above pylorus" and "near cardia", involved wall was not specified).		
Distance from Pylorus		
1-5 cm.	23	32
5-10 cm.	33	46
Near cardia	16	22

now being more frequently reported, as herein noted<sup>3,4,7,8,9</sup>. The long interval of time, 18 months, in one of the above patients further substantiates our opinion of careful, conservative medical treatment. Recurrent complaints need not bespeak for malignancy nor necessitate immediate surgery<sup>10</sup>, if the patient is under continuous medical observation.

#### CARDIAC AND PYLORIC ULCERS

Pyloric and prepyloric ulcers are more prone to malignancy than duodenal ulcers<sup>11,12,13</sup>. It is of interest to note that the ulcer was situated near the pylorus in 32 per cent of the patients (0.5 cm.) and further away towards the pars media in 46 per cent (5-10 cm. from pylorus). The cardiac region of the stomach always presents a difficult differential diagnosis roentgenologically between

benign and malignant lesions<sup>14,15,16</sup>. While the occurrence is infrequent, yet our series surprisingly reveals a gastric ulcer near the cardia in 22 per cent of the patients.

#### LABORATORY DATA

*Peripheral Blood Counts:*—No marked anemia was encountered in the non-bleeding ulcer patients both from the postmortem and surgical-pathological examinations. The lower hemoglobin values in the autopsied nonbleeding cases may be due to the more advanced age of the patient and the chronic diseases encountered<sup>17</sup>. These latter findings in the chronic diseased patients mostly caused by an arteriosclerotic artery, may account for the less pronounced anemia

TABLE V  
LABORATORY DATA IN BENIGN GASTRIC ULCER PATIENTS  
(AUTOPSY AND SURGICAL SPECIMENS)

a. Peripheral Blood Examination				b. Gastric Analysis						
Type	Number of Cases	Hb. (%)	RBC's (Millions)	Type	Free	Total	Percentage			
<i>Autopsies</i> (26)										
Nonbleeding	20	76.0	4.30	<i>Autopsies</i>	Not Performed					
Bleeding	6	62.0	3.22							
<i>Surgical Specimens</i> (34)										
Nonbleeding	31	83.5	4.50	<i>Surgical Specimens</i>	0	21	20			
Bleeding	3	36.0	2.12	Fasting						
				After Histamine	33	47	—			

observed in the bleeding autopsy cases than in the bleeding surgical ulcer patients. The marked anemia in the bleeding surgical ulcer cases undoubtedly is due to the acuteness of the condition (Table V,a).

#### GASTRIC ANALYSIS

No such determinations were noted in the patients studied from the postmortem material. As mentioned above the gastric ulcer was encountered as an incidental finding in many of these cases. In the operative patients, achlorhydria was found in 20 per cent of the cases, having an average total acidity value of 21 units. After histamine injection the values were: free 33 units, total 47 units. This shows the absence of hyperchlorhydria in some of the gastric ulcer patients (Table V,b).

Many observers believe gastric ulcer and duodenal ulcer to be two different entities and that the gastric ulcer patients reveal less acidity than the duodenal ulcer patients. We do not subscribe to this, since a previous publication by us revealed hyperacidity in only 58.8 per cent of peptic ulcer patients. There was practically no difference in the acidity values between gastric and duodenal ulcers patients<sup>18</sup>.

#### FECAL EXAMINATION

The intensity of the positive reaction will usually signify the extent of bleeding. The positive stool reaction occurred almost as frequently in the bleeding postmortem cases (15.4 per cent) as in the bleeding surgical cases (19.2 per cent). Negative stool specimens occurred in 23 per cent of the operative patients. It is of interest to note a positive stool reaction in such a

TABLE VI  
FECAL OCCULT BLOOD IN BENIGN GASTRIC ULCER PATIENTS

Type of Cases	Negative	Percentage	Positive	Percentage
Postmortem	2	7.7	(5)	(19.0)
Nonbleeding	—	—	1	3.9
Bleeding	—	—	4	15.4
Surgical Specimens	6	23.0	(13)	(50.0)
Nonbleeding	—	—	8	30.8
Bleeding	—	—	5	19.2
Total	8	30.0	18	70.0

large percentage of nonbleeding ulcer patients upon whom surgery was performed (30.8 per cent). A one and two plus Benzidine reaction was found only in the operative patients having a peptic ulcer history from 1½ to 7 years. The four plus Benzidine reaction in the postmortem cases was a result of a ruptured arteriosclerotic artery; an esophageal vessel, and not directly the result of the gastric ulcer per se as contrasted to the surgical patient (Table VI).

#### ROENTGENOLOGICAL FINDINGS

No mention is made of x-ray findings herein since our study was approached and corroborated by pathological examination rather than clinical. It becomes the duty of the physician, however, when treating patients with gastric ulcer to be guided by repeated and improved roentgenological changes in addition to his other observations. The patient is observed four to six weeks after the diagnosis is made. At the end of this time a repeat examination and x-rays are taken to note improvement clinically and roentgenologically as follows<sup>19</sup>:

- a) disappearance or diminution of the gastric deformity
- b) improvement in the general roentgenological signs
- c) absence of persistent reaction for occult blood
- d) gastric analysis especially achlorhydria.

#### COMMENT

There is no unanimity of medical opinion regarding the treatment of gastric ulcers<sup>20</sup>. Previous statistics reported the greater tendency of gastric ulcer to malignant degeneration. Many surgeons advised immediate operation influenced by reports of certain investigators<sup>6,10,21</sup>. There has recently appeared observations of the benignity of gastric ulcers particularly those encountered on the gastric greater curvature<sup>2,3,4,18</sup>. Even recurrent gastric ulcer does not necessarily mean surgery as previously advocated, but careful watching since a very small incidence of malignancy is encountered<sup>4,22,23</sup>. The more frequent occurrences of benign gastric ulcers prompt us to more conservative medical treatment before surgical intervention is contemplated.

Old age is no evidence that gastric ulcers are malignant. The autopsy findings herein reported of scarred gastric ulcers of many years' duration that are incidentally encountered in 26 per cent of geriatric patients are evidence of healing and of the essential benignity of gastric ulcer. More than 22 patients (33 per cent) related a history suggestive of peptic ulcer more than five years' duration. The gastric ulcers were most frequently encountered on the lesser curvature (64 per cent). Benign gastric ulcers on the greater curvature were observed in only three patients (4 per cent). This infrequency concurs with those of others.

Hyperacidity is not a constant finding in benign gastric ulcer patients. Fecal examination for occult blood may be observed in nonbleeding and even in benign gastric ulcer patients. Achlorhydria may be a temporary finding in gastric ulcer patients and should not be considered as such until the histamine injection test is performed. A peripheral blood examination may show more anemia in the aged than younger individuals with benign gastric ulcers. This may be due to the concomitant chronic diseases encountered such as leukemia, cirrhosis, arteriosclerosis, etc. It need not bespeak definitely for a malignant gastric ulcer.

Gastric analysis per se does not always help since free acidity may be encountered in malignancy<sup>18</sup>. Gastroscopy may be of help in a certain percentage of cases. The size of the niche larger than 1 inch in diameter does not always mean malignancy<sup>14,19</sup>. The presence of gastric and duodenal ulcers at the same time does not always exclude malignancy nor does the presence of an active duodenal ulcer with gastric ulcer<sup>24</sup>.

## SUMMARY AND CONCLUSIONS

1. Seventy-two patients with gastric ulcer confirmed at operation and encountered at postmortem examinations are herein presented.
2. Only 27 patients (37 per cent) operated for gastric ulcer presented a definite peptic ulcer history.
3. Benign gastric ulcers may be encountered in the cardia, pylorus and greater curvature of the stomach.
4. Nonmalignant gastric ulcers may occur in patients of advanced age.
5. The length of time of medical treatment does not preclude benignity of gastric ulcer.
6. Gastric acidity values need not differentiate gastric and duodenal ulcers.
7. Gastric ulcer when treated conservatively must be under constant surveillance.
8. Surgery is advised for gastric ulcer patients when definite criteria as mentioned herein fail.

## ACKNOWLEDGEMENTS

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## RECURRENT SMALL BOWEL OBSTRUCTION DUE TO DEVELOPMENTAL ANOMALIES IN ADULTS\*

### A PRELIMINARY REPORT

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Recurrent small bowel obstruction due to developmental anomalies† occurs more frequently than is diagnosed clinically or roentgenologically. By surveying its already known symptomatology and describing new findings it will be shown that it can be readily diagnosed.

The intention of this paper is not to review the literature. Only those publications will be quoted which have provided the authors with essential information.

Moynihan<sup>29</sup>, Huntington<sup>20</sup>, and Frazer and Robins<sup>11</sup> gave a clear account of the anatomical and embryological aspect of the subject. They reviewed the rotation of the gastrointestinal tract and the development of peritoneum, mesentery and mesocolon and also reported such developmental anomalies as the internal herniae, peritoneal folds, peritoneal fossae, congenital bands, and adhesions—anomalies which are often responsible for R.S.B.O.D. Moynihan has also critically appraised the literature and Huntington outlined the comparative anatomy and embryology of the gastrointestinal tract and peritoneum.

Surgeons (Bender<sup>3</sup>, Dott<sup>8</sup>, Gardner and Hart<sup>13</sup>, Callander, Rusk and Nemir<sup>6</sup>, Mandl<sup>23</sup>, Wakefield and Mayo<sup>39</sup>, Hansman and Morton<sup>19</sup>, Moretz and Morton<sup>28</sup>, Ripstein and Muller<sup>33</sup>, Brown and Ross<sup>4</sup>, McKechnie<sup>25</sup>, Nathan and Moseley<sup>31</sup>) accumulated knowledge of R.S.B.O.D. by studying the ileus caused by internal herniae, congenital bands and adhesions, long and short mesenteries, and congenital gaps in the mesocolon and mesentery.

The pediatrician's (McIntosh and Donovan<sup>24</sup>) contribution was through experience with the ileus of the newborn and infant, accounted for by volvulus of the small bowel secondary to lack of or insufficient fusion of the mesentery. In these cases one also encounters congenital adhesions in the area of the duodenojejunal junction.

The roentgenologist's increasing interest in the subject dates back to 1921 when Kummer (quoted by Exner) was the first to publish the roentgenological signs of the duodenojejunal hernia. Case and Upson, Taylor (quoted by Exner<sup>10</sup>),

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†Henceforth the abbreviation R.S.B.O.D. will be used.

Alexander<sup>1</sup>, Nathan and Moseley<sup>31</sup> were among the others who made contributions.

In the recent literature the papers of William and Hewes<sup>41</sup> and Parson<sup>32</sup> deserve to be stressed. Both papers reported on the roentgenological aspect of the internal hernia and emphasized its close clinical and roentgenological relation to the adhesions. Additionally, William and Hewes depicted the clinical picture of the internal hernia and Parson called attention to the frequent occurrence of the small and transient internal herniae. Parson attached to his paper a valuable bibliography which we have used profusely.

Based on the literature and our limited experience we shall view the R.S.B.O.D. as an entity. The underlying anomalies are all of the same origin and are formed by the defective rotation of the gastrointestinal tract, and defective development of the peritoneum. They are related to each other and follow certain anatomical patterns similar to the anomalies of the congenital heart lesions. If we find one anomaly, we can expect others.

This is a preliminary report of 13 patients with recurrent small bowel obstruction which we thought were due to developmental anomalies. They were all adults, well nourished, ambulatory, not acutely ill, and afebrile. Most of them did not offer any history of diarrhea. Their complaints were intermittent and of many years' duration. All laboratory findings were negative.

The patients could be divided into two groups. In the first group abdominal gas complaint predominated. The characteristic symptoms were rumbling or distention all over the abdomen or in a circumscribed area induced by a meal, physical strain, or a certain position (walking or standing). During the bouts, which lasted from a few minutes to several days or weeks, the patients had difficulties in expelling gas or were not able to expel gas for hours. In order to get relief they had to lie down, turn to one side or the other, double up or walk, or massage the abdomen. Not infrequently abdominal cramps, nausea and vomiting complicated the picture. These symptoms varied in intensity from slight distress to real misery. The majority of patients—who were for many years under medical care—sometimes of more than one physician—never told this story. They were not questioned adequately or did not think of gas as of any serious consequence or were embarrassed to tell about it. We obtained unrehearsed case histories by persistently repeated and pointed questions. In the second group the predominating complaint was nausea and vomiting precipitated chiefly by emotional upset and seldom by food. Two patients in this group had no other complaints. The third patient had the same complaints for many years, and lately she developed pains in the epigastrium and gas complaints. The first two patients and a fourth (not included in the table) made their own diagnosis: psychosomatic. Their roentgen findings will follow later.

The patients in the first group presented the following x-ray findings: Gas in the small bowel was one of the leading signs found on the scout film or on

TABLE I  
PERTINENT COMPARATIVE DATA OF 13 CASES OF RECURRENT SMALL BOWEL OBSTRUCTION

	Name & Age	Duodenal Loop	Duodenojejunal Junction Site of Pathology	Gas In Small Intestine	Site of Obstruction	Small Intestine Out-side of Ascending and/or Descending Colon	Previous operations	Other Diseases
1.	Mrs. P.R. -25	Dilated, Irritated	Normal Site, Sharply Angulated	++	Below Duodeno-jejunal Junction.	0	None	Duodenal Ulcer?
2.	Mrs. D.O. -54	Not Dilated, Irritated	Normal Site, Sharply Angulated	++	Below Duodeno-jejunal Junction.	0	Lumbar Sympathectomy.	Cholelithiasis. Hypertension.
3.	Mrs. I.M. -84	Not Dilated, Irritated	To Right of Mid-Line	++	Below Duodeno-jejunal Junction.	0	None	None
4.	Mrs. I.G. -56	Dilated, Irritated	Normal	++++	Left Mid-Abdomen.	Lateral to Descending Colon	None	None
5.	Mr. H.O. -48	Dilated, Irritated	Low	+++	Left Lower Quadrant.	Lateral to Ascending & Descending Colon	None	None
6.	Mrs. H.L. -49	Dilated, Irritated	Normal	+++	Left Upper Abdomen.	Lateral to Descending Colon	None	None

TABLE I (continued)

7.	Mr. L.C. —40	Dilated, Irritated	More to the Left than Average	0	Left Upper Abdomen, Right Mid-Abdomen.	Lateral to Descending Colon	None	None
8.	Mrs. H.O. —50	Dilated, Irritated	Normal	+++	Mid-Abdomen.	0	Cholecystectomy, Polyp in Rectum, Hemorrhoidectomy.	None
9.	Mrs. M.T. —60	—	—	+++	Right Mid-Abdomen.	0	Cholecystectomy, Partial Gastric Resection.	None
10.	Mrs. E.M. —55	Normal	Normal	+++	Right Mid-Abdomen.	0	Appendectomy, Cholecystectomy.	Diaphragmatic Ulcer
11.	Mrs. M.L. —25	Dilated, Irritated	Acutely Angulated	+++	Below Duodeno-jejunal Junction.	0	Appendectomy, Left Oophorectomy for chocolate cyst, Left Parabiliopancreatic Hernia (Acute ileus)	None
12.	Mrs. I.D. —40	Very Irritated	Normal	++	Adjacent to the Duodeno-jejunal Junction.	0	None	None
13.	Mr. J.L. —65	Normal	Normal	+++	Mid-Abdomen on Both Sides.	Lateral to Ascending & Descending Colon	None	Cirrhosis of Liver.

films taken for other abdominal examinations. We did not observe it on every film, but on most of them, whether or not the examination was done during a bout or a free interval. The gas in the small bowel was isolated in pool-like areas (Figs. 1a, 1b and 2b). The gas collections are not always in the same area (in the same patient) at different times during the examination. The gas collections are in segments of small bowel of varying sizes and shapes. Some are dilated and others are not. This is in contrast to the acute small bowel obstruction with continuously dilated gas-filled loops. In R.S.B.O.D. the gas-filled loops are not uniformly dilated. There may be varying degrees of dilatation, or none at all. With gas in the ileum the mucosal folds are obliterated most of the time. In the jejunum, the mucosal folds may or may not be obliterated (Fig. 3a). The presence or absence of folds has no relation to the caliber of the gas filled jejunum; the folds may be obliterated whether the loop is dilated or of normal caliber.

The gas filled small bowel loops can usually be distinguished from the large bowel. They are in the middle of the abdomen, their lumen is small in width, the valvulae conniventes in the jejunum have a characteristic feathery structure, and the ileum is smaller in width than the colon, and lacks haustration. Such a differentiation, however, is not always possible. In some cases the small bowel loops are lateral to the ascending or descending colon or are overlapped by a redundant sigmoid, hepatic or splenic flexure. In other cases small bowel loops can be as wide as the colon and show indentations indistinguishable from the haustra of the colon. A barium enema helps to make the differentiation.

By studying the x-ray films of the patients in the first group following administration of barium we learned to appreciate signs which we neglected before. Among these were such developmental anomalies as the mobile duodenum, the reversed duodenal loop, and the atypical location of the duodenojejunal junction (the duodenojejunal junction was on the right side, or too far from the midline on the left side of the abdomen, or it was too high or too low in position). We attach similar significance to a dilated duodenal loop and to an acutely angulated duodenojejunal junction. An upper jejunal loop, which crosses from the left side of the abdomen to the right and returns to the left can be the first indication of developmental anomalies. All these signs are in the upper abdomen. In the same area and in the remaining part of the abdomen we find anomalies involving the position of the large and small bowel. Atypically the entire large bowel can be found in the left abdomen and the small bowel in the right, or the colon can be fixed in any position which it occupied during rotation. For instance the cecum can remain in the mid-portion of the upper abdomen or in the right hypochondrium or somewhat lower. At the same time a part or the entire jejunum is on the right side of the abdomen and the ileum on the same or the other side. The relative position of different portions of the small bowel can vary considerably.

The most important direct sign of recurrent ileus is dilatation of the lumen proximally to a narrowed area involving one or several loops in any part of the abdomen. If it is in the left upper abdomen it suggests a developmental origin (Figs. 1c and 4b). A discussion of this problem will follow below.

Internal herniae, bands and adhesions also cause other characteristic x-ray findings. These anomalies can force the loops to be closely grouped and crowded. They remain so during the entire examination and also with the patient in different positions.

Irritability can be encountered in the narrowed, dilated and crowded loops and also in the more distant loops. (The term disturbed physiology will be used interchangeably with irritability). It is characterized by lack of physiological harmony of the mucosal pattern; the width and the outline of the loops is slightly irregular and sometimes rigid. The distribution of barium in such an area is dysharmonic and is called segmentation, fragmentation, flocculation, scattering, etc. Hypo- and hypermotility are also signs of irritability.

There were five patients in the first group with additional characteristic findings: Several small intestinal loops were located lateral to the ascending or descending colon (Figs. 3a and 3c) or both. These and the neighboring loops medially to the colon contained gas and showed irritability. Some of the loops were dilated (Fig. 3b). These signs indicated an obstruction.

The x-ray findings of the patients in the second group were striking. The duodenum and the upper jejunal loops were considerably and continuously dilated (Fig. 4b). There was irritability of the mucosa in the same loops and narrowing of the lumen distal to the dilated loops. These findings were similar to that of an acute small intestinal obstruction, and they were present whether or not the patients had any clinical symptoms.

For a small bowel study our patients drank 3 eight ounce glasses of barium mixture. Each glass contains one heaping tablespoonful of "I-X barium unflavored" dissolved in tap water. They drank it in 15 to 20 minutes during the examination of the upper gastrointestinal tract. Films are taken at half hour intervals from five to eight hours. It is advisable to continue with the examination as long as there is barium in the small bowel. Supplementary examinations of the lower part of the small bowel by a barium enema may also furnish additional information.

Four representative cases from a group of 13 have been selected and they will be described here. Comparative data evaluating all 13 histories can be found in the table below.

*Case 1:*—H.O., female, age 50, well nourished, complained of considerable distention, "blockage" in the left upper abdomen. She could expel gas only while lying on her right side. Had a normal appetite and regular bowel move-

ments. Had a hemorrhoidectomy in 1950, 6 months later a cholecystectomy, and in 1952 polyps were removed from the rectum. Several gastrointestinal series and barium enemas were made elsewhere. She was told that she had nervous intestine. Review of these films were negative for intrinsic pathology of the stomach and large intestine. Because of the presence of a large amount of gas in the small intestine (Fig. 1a) we repeated the gastrointestinal series in April 1953, with special reference to the small intestine. The postevacuation film following a barium enema showed an increased amount of air in both sides of the abdomen, lodged partly in small intestinal loops (Fig. 1a). The valvulae conniventes were absent in some of the gas-filled jejunal loops whether the loops were dilated or not. On the 1 hour small intestinal film there was moderate dilatation and irritability of the duodenal loop and the proximal part of the small intestine appeared normal in pattern, width and outline (Fig. 1b). On the 1½ hour film some of the small intestinal loops were pathologically dilated, irregular in width and outline, and contained barium or gas (Fig. 1c).

*Diagnosis:*—Internal hernia. Operation revealed the following: The stomach, omentum and splenic flexure were found adherent to the anterior abdominal wall. About 6 inches of the terminal ileum was adherent to the cecum. A paraduodenal fossa about 3½ inches in depth was found just to the left of the ligament of Treitz. On approaching the paraduodenal area a segment of the jejunum about 6 to 8 inches in length was found to be distended and yellow in color. After about 5 minutes the distention disappeared and the color returned to normal. The jejunum immediately distal to this segment was collapsed. The adhesions were mobilized. The paraduodenal fossa was obliterated.

*Case 2:*—P.H.O., male, age 48, had abdominal episodes about twice a year for the past few years. These episodes started either with abdominal distention or nausea. These two symptoms combined in some instances and were accompanied by pain. After the episodes subsided, abdominal tenderness persisted for several days. Each episode lasted 15 to 20 minutes, and was preceded by weakness and profuse perspiration. Relief was obtained by expelling gas or bowel movements. Lately he has had two attacks, the first lasted two hours and the second two days with fluctuating intensity. Diarrhea following administration of Telepaque tablets for a gallbladder examination brought considerable relief. Appetite and weight were normal and bowel movements were regular. There was no abdominal operation. A gastrointestinal series including small intestinal studies on Feb. 3, 1954, showed: On the ½ hour film the mucosal pattern in the stomach, duodenum, and jejunum was normal (Fig. 2a). The duodenojejunal junction was somewhat lower in position than the average and also somewhat displaced to the left. There was a large amount of gas in the small intestine on the right side. On the 1, 1½, and 2 hour films the duodenum was somewhat dilated and irritated. From 3 to 5 hours after intake of barium there was a large amount of gas in the small intestine on the left side. Distal to this area there was a pathologically dilated small intestinal loop (Figs. 2b and 2c). It should

be noted that on the  $\frac{1}{2}$  hour film the small intestine appeared to be normal in the same area. Films showed some jejunal loops lateral to the descending colon and some loops of the ileum lateral to the ascending colon.

*Diagnosis:*—Recurrent partial obstruction of the small intestine secondary to developmental bands and a long mesentery.

*Case 3:*—H.L., female, age 49, complained for the past 2 years of constant nausea of increasing severity, pain in the epigastrium unrelated to food intake and constipation. A gastrointestinal series and small intestinal study on July 3, 1953 and a barium enema on June 27, 1953, revealed: On the barium enema film there was a large amount of gas in several jejunal loops (Fig. 3a). Some of them were lateral to the descending colon and displaced the descending colon

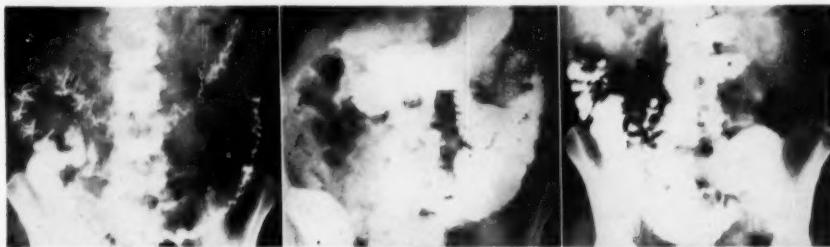


Fig. 1a

Fig. 1b

Fig. 1c

Fig. 1a—Postevacuation film following a barium enema shows an increased amount of gas in the small intestine in the left abdomen. Some of the loops are dilated.

Fig. 1b—1-hour film shows moderate dilatation and irritability of the duodenal loop. Normal proximal small intestinal loops. Large amount of gas in the small intestine on the right side.

Fig. 1c—6-hour film shows dilated, isolated small intestinal loops. Some are filled with gas others with barium. Some of these loops appeared normal on the 1 hour film. See Fig. 1b.

medially. Only a few of the gas containing jejunal loops showed valvulae conniventes (Fig. 3a) in spite of the fact that the loops were not dilated. On the  $\frac{1}{2}$  hour film some of the jejunal loops were dilated (Fig. 3b). Three hours later there was marked irritability of the small intestine in the same area. There also was a large amount of gas in some of the small intestinal loops which again displaced the descending colon medially (Fig. 3c).

*Diagnosis:*—Internal hernia, or a band, or a gap in the mesocolon. The patient underwent a surgical exploration, which did not reveal any pathological changes. Special attention was paid to a possible gap in the descending mesocolon. Such a gap could not be found. To explain the roentgenological findings we assume that a long mesentery allowed the small bowel loops to be lodged laterally to the descending colon and a long descending mesocolon allowed the descending colon to be displaced by small bowel loops medially. Mutual pressure

of the descending mesocolon, descending colon, mesentery and small bowel can account for the small bowel obstruction.

**Case 4:**—P.R., female, age 25. For the past 7 years had vague annoying sensations in the epigastrium which radiated upward along the anterior chest to the throat, occasionally with nausea and vomiting. They lasted 3 to 5 days with varying intensity and were brought on by emotional upsets rather than food. Lately these attacks were more frequent and more severe and occurred about every 2-3 months. The last attack was one month prior to the x-ray examination. The longest was during her summer vacation and lasted 10 days. X-ray examination of the gastrointestinal tract and a small intestinal study on Dec. 29, 1953, revealed a deformed bulb and a duodenal loop which was dilated and irritable (Fig. 4a). There was an acute angulation of the duodenojejunal junction



Fig. 2a

Fig. 2b

Fig. 2c

Fig. 2a—30-minute film. The proximal loops of the small intestine are normal in width and outline and present a normal mucosal pattern. There is an increased amount of gas in several loops of the ileum.

Fig. 2b—3½-hour film. There is a large amount of gas in the jejunum. Distal to this area there is a markedly dilated small intestinal loop.

Fig. 2c.—4-hour film. There is progressive dilatation of the same small intestinal loop as described in Fig. 2b. There is still a large amount of gas proximal to this area.

and extrinsic pressure against the jejunum. Distal to this area the small intestinal loops were moderately dilated and the mucosal pattern represented border line changes between normal and pathological. On the 2½ hour film one recognized a pathologically dilated small intestinal loop with marked narrowing on the left side below the duodenojejunal junction (Fig. 4b). There were also gas-filled irritated jejunal loops in the left half of the abdomen. On the 3½ hour film there was a large amount of gas pooled in the small bowel and localized in the left upper abdomen.

*Diagnosis:*—Small intestinal obstruction due to internal hernia or bands.

#### COMMENT

Our series is not large enough to be of statistical value, but it is worthwhile to know that we collected 13 cases of R.S.B.O.D. within a period of a year. During the same period we recognized 45 cases of peptic ulcer in the stomach and

duodenum and 21 cases of biliary calculi. These figures are included only to show the relative frequency of R.S.B.O.D. with well known ailments of the alimentary tract. The figures indicate that the R.S.B.O.D. is common.

Surgeons (Wakefield and Mayo<sup>39</sup>, Brown and Ross<sup>4</sup>, etc.) stress how often mesenteric bands and congenital adhesions precipitate small bowel obstruction. The surgical cases, however, including the internal herniae, represent only a small fraction of the cases of R.S.B.O.D. which are in nonsurgical care.

R.S.B.O.D. often remains unrecognized for several reasons. Many patients are reluctant to complain about gas distention or difficulties to expel gas. Frequently the x-ray films showed pronounced gas collection in the small bowel



Fig. 3a

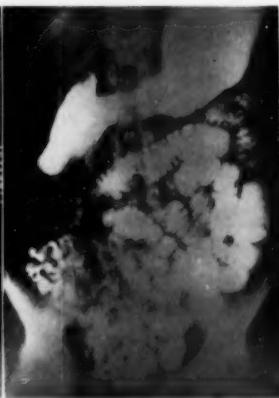


Fig. 3b



Fig. 3c

Fig. 3a—Barium enema film shows displacement of the descending colon by gas filled jejunal loops. Note that only a few jejunal loops show valvulae conniventes. Valvulae conniventes are not always visualized whether loops are dilated or not.

Fig. 3b—1½-hour film. Intestinal loops showing dilatation as well as disturbed physiology.  
Fig. 3c—4½-hour film. The descending colon is displaced medially by gas filled small intestinal loops. There is also gas in the small intestine medial to the descending colon.

and after we questioned them repeatedly the patients admitted their complaints. One patient called us the day after the examination to confess that she misled us by denying her gas complaints. The bouts of gas distention might be brief and not very irritating. Even if they are distressing they subside most of the time without medical help or any consequences. Therefore, the patients remain unconcerned and feel more relieved by such ill-founded diagnoses as gas pain, gas pocket, nervous intestine and spasm.

The confusing interpretation of gas in the small bowel is another source of diagnostic error. Ritvo and Shauffer<sup>34</sup> gave an excellent survey on this subject and stated that the importance of gas pattern in the intestine cannot be overemphasized. A basic principle should be that whenever gas is in the small bowel

its cause must be investigated. We cannot always find it but more frequently we can. It is bad practice not to evaluate the gas in the small bowel scrupulously because aerophagia and many other factors may produce it. Asthma, infectious disease, morphium injection, renal or biliary colic, injuries to the spinal column, acute inflammatory disease, pancreatitis, appendicitis, cholecystitis, ileojejunitis, amyloidosis and sarcoidosis of the small bowel and intravenous pyelography can be associated with gas in the small bowel. But all these conditions can usually be separated from recurrent bowel obstruction.

Gas due to recurrent obstruction is pooled in the small bowel in segmented loops, which may or may not be dilated. Other appropriate terms for the same sign are: stasis, stagnation of gas, or delayed propulsion of gas in the small bowel. This is in contrast to the gas-filled and continuously dilated small bowel

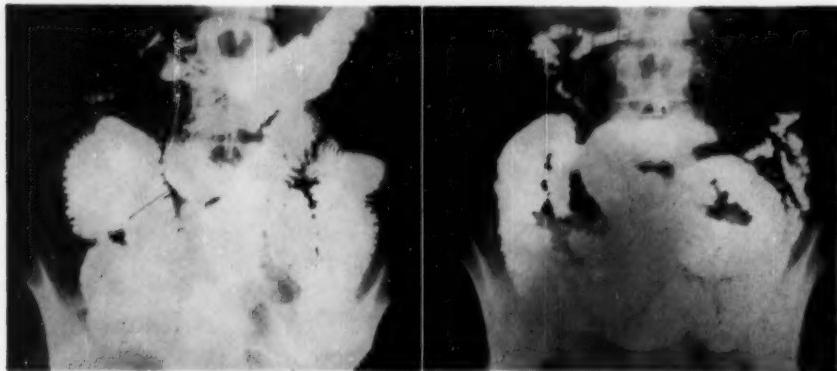


Fig. 4a

Fig. 4b

Fig. 4a—30-minute film. Deformed bulb, dilated and irritated duodenal loops. Sharply angulated duodenojejunal junction.

Fig. 4b—2½-hour film. Markedly dilated small intestinal loops with distal constricted area on left side, below the duodenojejunal junction. Irritated gas filled jejunal loops in upper half of abdomen, left side.

loops in acute small bowel obstruction. It should also be stressed that often a barium enema is necessary to determine whether the gas is in the small bowel or in a redundant splenic or hepatic flexure or sigmoid.

Gas complaints with gas in the small bowel indicate an obstruction irrespective of its origin. An intrinsic pathological change, extrinsic hernia, and extrinsic mass (tumor, aneurysm, abscess, enlarged abdominal organs) have to be ruled out before we think of developmental anomalies as responsible for the obstruction.

We have already enumerated a long list of the developmental anomalies and do not wish to repeat it here. We also will not review the complete embryology of the intestinal tract and peritoneum, although a thorough knowledge of it is essential to understand the anomalies. A review can be found in several

publications mentioned in the introduction of this paper. We will, however, touch upon a few changes which lead to the developmental anomalies and explain why most of these are in the duodenojejunal and adjacent area.

In the early phase of the development the umbilical loop from which the small bowel and part of the large bowel develop is firmly fixed at its two ends to the posterior abdominal wall. These two points are in the duodenojejunal and adjacent areas and around these points the following parts of the intestinal tract pivot trailed by the corresponding sections of the mesentery: 1. stomach and duodenum as they turn from the mid-line position to the right side, 2. small bowel as it moves from the right side of the abdomen into the left, 3. ascending and transverse colon as they move from the left side of the abdomen into a transverse position in the upper abdomen, 4. descending colon as it moves from a median position into the left side of the abdomen. While these changes are taking place the mesentery throws folds around the points of fixation. These folds form many of the peritoneal folds and pouches seen in adults. In the same area fusion takes place: 1. between the distal part of the transverse mesocolon, the upper part of the root of the mesentery and the peritoneum of the posterior abdominal wall, 2. between the greater omentum and the transverse colon. The fusion occurs with the help of the connective tissues. The process is similar to the bony union of a fracture which sometimes develops an excessive amount of bony callus. An exuberant amount of connective tissue at the sites of the peritoneal fusion results in adhesions.

All these changes are synchronized and planned in space. Each change is part of one firmly fit system. By altering one part or the pace of one event we may bring about one anomaly or a chain of anomalies. For instance, the migration of the ascending and transverse colon from the vertical position in the left side of the abdomen into the transverse position in the upper abdomen is synchronized with the migration of the small bowel from the right side into the left. If the ascending and transverse colon move faster they may envelop with their mesocolon, one part or the entire small intestine and thus produce a so-called retroperitoneal hernia.

Retention band (traction band) is a condensation of connective tissues, which connects the posterior abdominal wall in the area adjacent to the duodenojejunal junction with 1. the distal part of the transverse colon, 2. with the Treitz ligament, 3. the cecum, 4. the primitive descending mesocolon. This band plays an eminent part in guiding the rotation of the intestinal tract. At the end of the embryonic life it usually disappears, however, it may persist in adults as a more or less extensive peritoneal band.

Each of the above changes should be understood and the amazing number of changes appraised in the duodenojejunal and adjacent areas to be able to appreciate the sources and nature of the developmental defects. There is a statistic (Hausman and Morton<sup>19</sup>) which indicates that 70 per cent of the

internal herniae are in that area and it is reasonable to assume that developmental bands and adhesions are just as frequent here.

Similar but not as many changes are taking place in other areas of the abdomen: in the ileocecal, sigmoid area, around the foramen of Winslow and elsewhere.

The unusual size of the mesentery (short and long mesentery), the pathology of the fanlike or plaited structure of the mesentery complete the list of anomalies responsible for R.S.B.O.D.

Two types of R.S.B.O.D. are of special interest. The first has been classified above as the second group of our cases, comprising 3 patients. Their principal symptoms were intermittent nausea and vomiting. Two of them were 25 years old, the third 40. Their complaints started when they were young, the first was 18, the second 14, and the third 20 years old. Recently we examined a fourth patient (not included in the table) in the same category. She is 18 and has a history of short duration. All four are females.

Roentgenologically in these four cases we found the duodenum and in its continuation several upper jejunal loops dilated and irritable. In the same area there were short stretches of narrowing which measured 1-2 cm. in length. The narrowed stretches were probably produced by bands because the mucosal pattern was well maintained. Two of these patients were surgically explored and in both cases paraduodenal herniae were found. We x-rayed the first case before the operation, and the second several weeks after operation. We were surprised to find roentgenologically in this second case the same changes as in the first, although the surgeon had reduced the hernia. Parson<sup>32</sup> observed a similar case (his Case 2). We can only speculate as to the postoperative findings in this case. It is possible that some of the obstructive bands were not detected and not severed or a peculiar alignment between the mesentery and small bowel kept the loops in unchanged position. Three of these 4 patients were free of complaints at the time of the x-ray examination. One of them was free of complaints more than a month before the examination. It is characteristic of these patients to have permanent roentgen signs of incomplete obstruction whether they have complaints or not. An unknown factor has to be added to induce the complaints. In three of the four patients emotional upsets precipitated the vomiting spells. One of the patients told us that vomiting spells were brought on at three different occasions by a miscarriage, a death, and a serious illness in the family. Another complained of vomiting whenever her boyfriend called on her. The first patient considered herself as "psychosomatic". Psychotherapy was recommended to the second patient by an expert, who refused to believe that a bowel obstruction could precipitate such symptoms. The third patient simply stated that aggravation induced her to vomit. Our belief that there is a causal relationship between the dilated duodenal and upper jejunal loops and vomiting is supported by cases which Ross Golden mentioned in "Diagnostic

"Roentgenology" under chronic duodenal stasis produced by developmental bands. The symptoms he mentioned: psychogenic disorder, anorexia nervosa, and weight loss are identical with those of our patients.

It seems to us that our three patients whom we have classified as the second group represent a roentgenological and clinical entity.

The second type of R.S.B.O.D. which is of special interest is represented by five cases which are included in our first group. It is characterized by small bowel loops located laterally to the descending or ascending colon or to both. These loops and those medial to the colon are filled with gas, some of them are dilated and others not. This finding is called gas pooled in bowel loops or stagnation of gas, and is characteristic of delayed transportation or impaired propulsion of gas, and represents incomplete obstruction. The barium in these loops shows irritable mucosa. This anatomic relation of the colon and small intestine can be seen if there is a gap in the mesocolon which permits small bowel loops to pass through. Many such cases are reported in the literature. One of our cases of this type was operated on and no such gap was found. In this case we found marked displacement of the descending colon medially at two separate examinations in addition to the x-ray signs just described. We assumed that either the descending mesocolon or the mesentery or both were too long and allowed the corresponding intestine to move in an unusual position. This mechanism which is accompanied by mutual pressure of the small and large bowel, mesentery and mesocolon may produce the symptoms and roentgenological signs of recurrent obstruction. This type of R.S.B.O.D. was recognized accidentally. We noticed the above x-ray findings in several cases and by questioning the patients we gathered that they had the symptoms of recurrent bowel obstruction.

We already discussed the surgical findings of three patients, here we add those of a fourth. The patient is included in the table as Case 10. She had irritable, fixed small bowel loops with narrowed and dilated segments in the right mid-abdomen. There was also gas pooled in the small bowel in both sides of the abdomen. Our diagnosis was adhesions or internal hernia. Years before the patient underwent a cholecystectomy for calculi. At the same time the appendix was also removed. Gallstones were found at this operation which relieved the patient from typical gallbladder colics. The constant pain throughout the abdomen which annoyed the patient many years before the operation, however, remained unchanged thus preventing her from bending and doing housework. A subsequent exploratory revealed the duodenum adherent to the undersurface of the liver and the liver adherent to the abdominal wall below the umbilicus. Adhesions to the colon were also in this area. The mesentery was fixed in the right lower quadrant to the lateral abdominal wall at the site of the previous appendix operation. There was one adhesion band between the sigmoid and omentum. The small bowel was negative for intrinsic pathology. The extent and location of the adhesion bands suggest that they were mostly congenital in origin.

They fulfilled the requirements of Wakefield and Mayo<sup>39</sup> who postulated that in adults only those bands can be designated as congenital which are at sites where bands can be found during embryonic life. This is in contrast to adhesions due to peritonitis or postoperative adhesions which are irregularly distributed. In view of previous operations, however, we cannot rule out postoperative adhesions.

This case and others (our own and from the literature) were quite instructive. We could not find any statistics as to the frequency of R.S.B.O.D. or the frequency of all the individual anomalies which could be responsible for R.S.B.O.D. Related to this problem is the acute small bowel volvulus due to developmental anomalies about which there are statistics. Brown and Ross<sup>4</sup> stated that 10 per cent of the cases operated for bowel obstruction have some gross anomaly of the intestinal rotation or mesenteric attachments. In a large number of these cases the small bowel is involved. Moretz and Morton<sup>28</sup> found in 36 cases of acute volvulus of the small bowel that 11 did not have any previous laparotomy. Among the latter, 7 had fibrous bands probably congenital in origin and 2 had fibrous bands between a Meckel's diverticulum and the anterior abdominal wall. McKechnie<sup>25</sup> found that in 30 cases of acute volvulus of the small bowel 10 were due to congenital anomalies. Since R.S.B.O.D. is even more prevalent than acute small bowel obstruction we believe that it is a frequent entity. Because of its frequency and also because the surgical approach and prognosis are different (Ladd<sup>21</sup>) in bowel obstruction due to developmental anomalies from those in bowel obstruction due to postoperative adhesions, and adhesions due to peritonitis, it is desirable to improve our diagnostic acumen. Thus, preoperatively, we shall be able more often to arrive at a correct diagnosis. This case is one of a group of cases in which the R.S.B.O.D. was not recognized and the patient was operated on for biliary calculi. In other instances R.S.B.O.D. was mistaken for disease of the stomach, gallbladder, and appendix and operations performed on these organs. If such cases are eventually reoperated for R.S.B.O.D. the developmental adhesions which were overlooked at the original operation might, or will be erroneously considered as postoperative adhesions.

#### SUMMARY

A preliminary study on 13 patients revealed that recurrent small bowel obstruction produced by developmental anomalies occurs frequently in adults. It is characterized by episodes of 1. abdominal distention, 2. difficulty or inability to expel gas, 3. pain in the abdomen, 4. nausea and vomiting.

Roentgenologically the most frequent signs are: 1. circumscribed widening and/or narrowing of one or several loops of the small bowel, 2. gas in the small bowel.

These unspecific findings are qualified to be developmental in origin by the following x-ray changes: 1. Anomalies of the intestine due to faulty rotation,

2. anomalies due to faulty fusion of the primitive peritoneum with the primitive mesentery and mesocolon (mobile duodenum, unusual position of the duodenojejunal junction, dilated duodenum, etc.) 3. localization of a small bowel obstruction in the vicinity of the duodenojejunal junction where the majority of those developmental anomalies which produce obstruction occur.

Two groups out of the reported 13 patients are of additional interest. In the first group—comprising 3 patients—nausea and vomiting were the dominant symptoms and dilatation of several upper jejunal loops were the characteristic roentgenological signs of obstruction. In the second group—comprising 5 patients—gas containing small bowel loops situated lateral to the ascending and/or the descending colon caused investigation for obstruction. It was assumed that mutual pressure of the small bowel, colon, mesentery and mesocolon on each other caused an obstruction.

The first group represents a clinical and roentgenological entity and the second a roentgenological entity.

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## *President's Message*

As the new President of the American College of Gastroenterology, I extend to you my greetings.

The American College of Gastroenterology has prospered under prudent administration these past few years. The officers for 1955-56 will endeavor to accelerate its growth. The College is unique among medical societies; it is a common meeting ground for men from all sections and specialties interested in gastroenterology. While it is primarily a clinical group, professors and experimental surgeons are prominent on its membership rolls. Radiologists, proctologists, general practitioners, internists, and general surgeons alike have contributed to its development. Future horizons are unlimited.

The Board of Trustees has done an exceptionally fine job in permitting the influx of young men with new ideas into the group. This strength in depth will serve well in years to come. Constructive criticism from the entire membership will be welcomed. Several men have already suggested that the College require attendance at a certain percentage of its conventions and regional meetings. This thought is in line with the idea that the privileges of affiliation must be associated with responsibility for continued education in the expanding field of gastroenterology. It has been presented through me for your consideration.

I deeply appreciate the privilege of serving as President of the College and shall do all in my power to merit this trust.



*J. J. Nix*

## NEWS NOTES

### NEW FELLOWSHIP KEYS



New Fellowship keys for Fellows of the American College of Gastroenterology have been authorized by the Board of Trustees. An illustration of the new key is at the left.

Fellows may order the new keys from the headquarters office, 33 West 60th Street, New York 23, N. Y., at \$10.00 each including federal tax and shipping charges.

The reverse side of the key will be engraved with the name and date of election to Fellowship. Send your orders in today.

## In Memoriam

We record with profound sorrow the passing of Dr. Grant H. Lanphere, Fellow, of Beverly Hills, Calif. We extend our deepest sympathies to the bereaved family.

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## BOOK REVIEWS FOR GASTROENTEROLOGISTS

**SYSTEMIC ASSOCIATES AND TREATMENT OF SKIN DISEASES:** Kurt Wiener, M.D., Dermatologist, Mt. Sinai Hospital, Deaconess Hospital, St. Michael's Hospital, Milwaukee, Wisc. 556 pages with 90 text illustrations. C. V. Mosby Co., St. Louis, Mo., 1955. Price \$17.00.

Here again is a book that is well written, beautifully printed and illustrated by an author who knows his subject.

Many skin manifestations according to Dr. Wiener are of systemic origin and require diagnostic acumen and well aimed treatment for eradication of the primary focus rather than the external manifestation. Diagnosis, symptomatology, medication including antibiotics, vitamins in addition to the external application of lotions, ointments, etc., are fully discussed. To acquaint the American physician, many drugs advocated abroad are mentioned and evaluated in a given case. On page 195, the author discusses urticaria and its many causes, allergy, drugs, serum, blood, foreign pro-

teins, inhalants, seasons. He further mentions the gastrointestinal tract, which includes the stomach, gallbladder, liver and appendix. Under incidence, he calls attention to sex and heredity. The reader will find excellent description of the various types of urticaria and treatment on page 203, etc.

Beginning with page 373, the physician will be pleased to note the introduction of the various preparations, such as ACTH, cortisone, hormones, sulfonamides, antihistaminic agents, metals, etc., etc.

The reviewer highly recommends Dr. Wiener's *Systemic Associations and Treatment of Skin Diseases* as a valuable asset to the physician's "must" books.

**VERHANDLUNGEN DER DEUTSCHEN GESELLSCHAFT FÜR VERDAUUNGS UND STOFFWECHSELKRANKHEITEN** (Transactions of the Society for Digestive and Metabolic Diseases). XVII Meeting held in Stuttgart-Bad Cannstatt und Bad Mergentheim, 24-27 September 1953: Prof. Dr. W. H. Bans, Hamburg. 340 pages, illustrated in black and white, diagrams and tables. Georg Thieme Verlag, Stuttgart, Germany, 1954. Price \$11.95.

In this paper-bound monograph containing the transactions and papers submitted at the meeting of the Society for Digestive and Metabolic Diseases, the physician who reads German will find many new theories, diagnostic methods and last but not least, treatment of diseases the human body is heir to. These papers are ably discussed and enhance the value of the transactions.

Heuming's paper on "Colitis Ulcerosa" and the several discussers added a great

deal of new knowledge to a disease which for many years baffled the medical profession. It is hoped that somebody, somewhere, will find inclination and time to abstract into English the salient points so that English speaking physicians may try to relieve patients suffering with ulcerative colitis.

Another chapter deals with cholangitis in all its phases including spa treatment of the chronic patient.

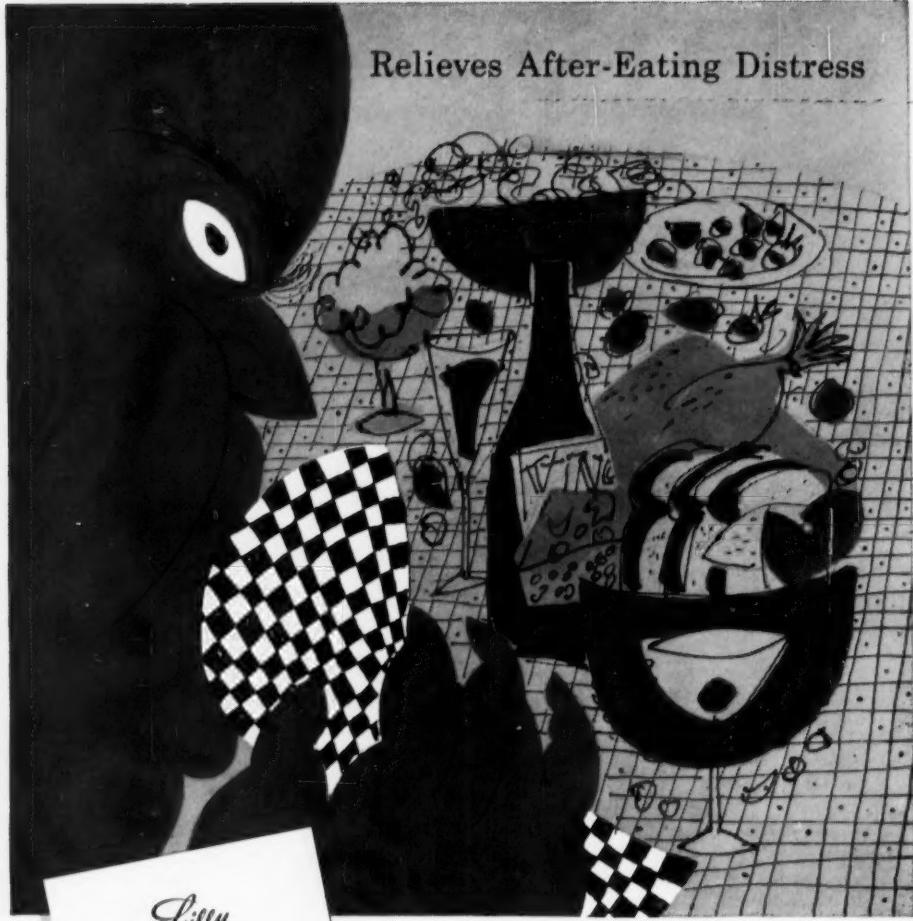
**PORTAL HYPERTENSION AND THE DUMPING SYNDROME:** IVth Congress of the National European and Mediterranean Gastroenterological Associations with the cooperation of the French National Society of Gastroenterology, Paris—June 27-July 2, 1954. 455 pages, illustrated. Masson & Co., Paris, France, 1954. Price 3,500 fr.

At this congress, portal hypertension, diagnosis and treatment was discussed. A complete exposé of the portal hypertension syndrome is found in the well-printed and illustrated treatise. The second subject presented and discussed was the "Dumping Syndrome" following gastric resection.

In this volume, the reader will find papers which were read in several languages and summaries of the presentations in German, English and French.

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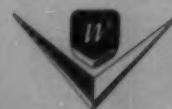
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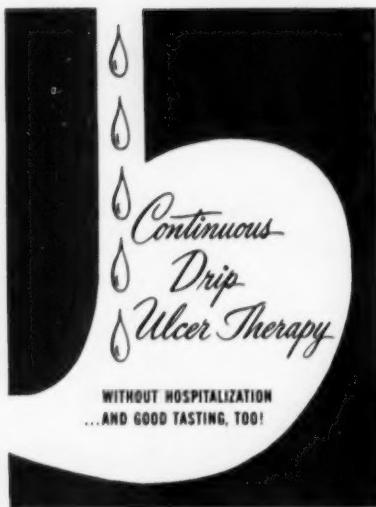
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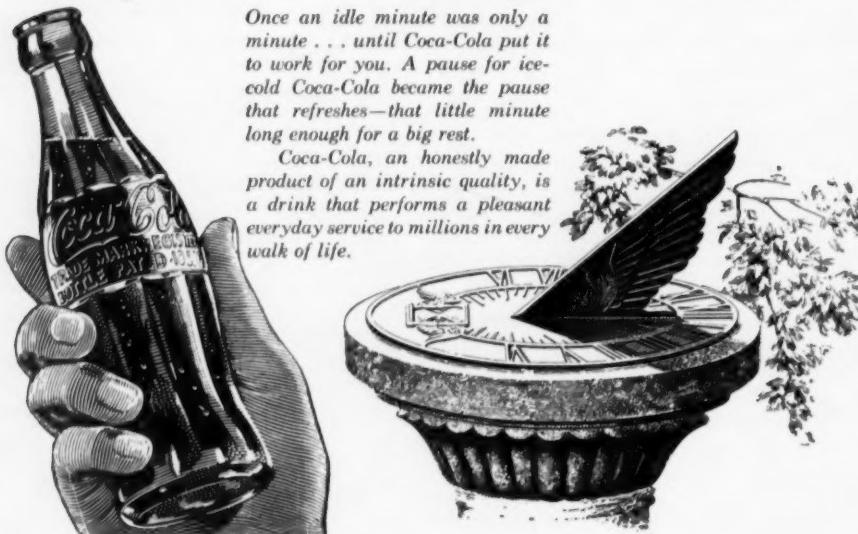
\*Steigmann, F., and Goldberg, E.: Ambulatory Continuous Drip Method in the Treatment of Peptic Ulcer, Am. J. Digest. Dis. 22:67 (Mar.) 1955.

†Mg trisilicate 3.5 gr.; Ca carbonate 2.0 gr.; Mg oxide 2.0 gr.; Mg carbonate 0.5 gr.

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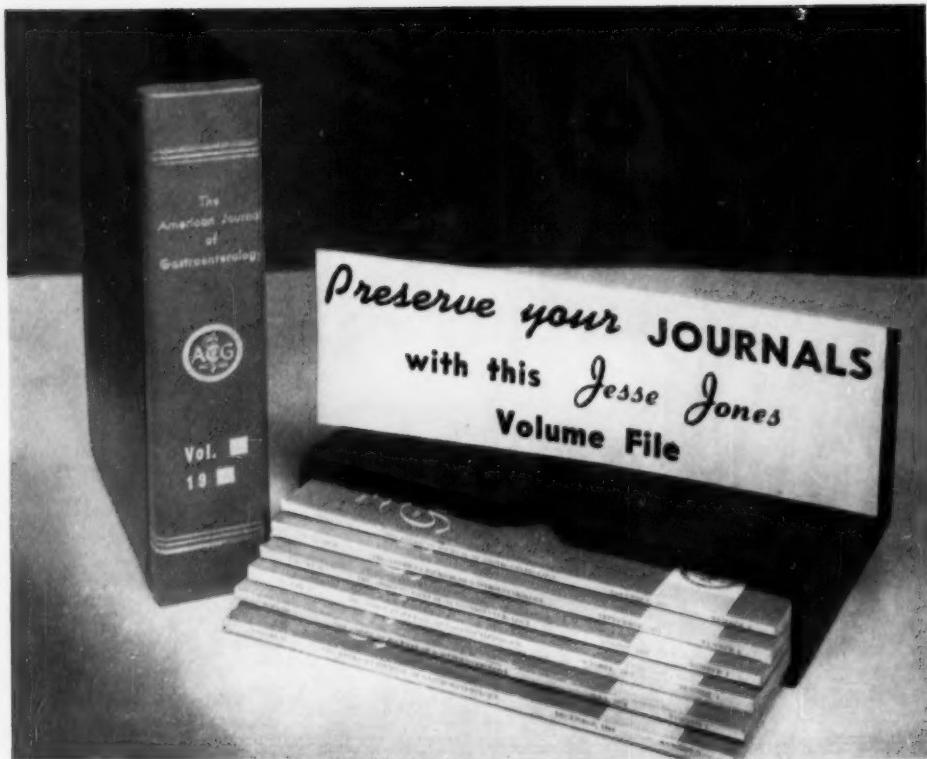
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1. Balfour, D. C., Jr.: Am. J. Gastroenterol. 22:181, 1954.  
2. Burke, J. O., et al.: Internat. Rec. Med. & Gen. Practice Clin. 167:587, 1964. 3. Sternberg, S. D., and Greenblatt, I. J.: Ann. Allergy 9:190. '64.

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No untoward effects have been observed in patients receiving Probutylin for as long as two years. It is contraindicated only in certain cases of hypertension.

#### SUMMARY OF A SELECTED CLINICAL STUDY

Treatment of gastrointestinal symptoms associated with the following:	NO. OF CASES	PERCENT COMPLETE SYMPTOMATIC RELIEF									
		10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Nausea and vomiting, hiccups, pylorospasm	104										80%
Hiatal hernia, gastro-duodenitis, upper gastrointestinal bleeding	15										87%
Gastritis medicamentosa	8										100%
Genito-urinary disorders	23										74%
Postoperative nausea and vomiting	15										90%
Nausea and vomiting of pregnancy	7										71%
Gall bladder disorders	10										80%

#### RECOMMENDED DOSAGE SCHEDULE

**Gastritis:** 1 or 2 capsules 20 minutes before meals and antacid (Maalox®) 20 minutes after meals.

**Post-alcoholic gastritis:** 2 capsules with antacid (Maalox®).

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## Mrs. Brown refused to sink

**K**EEM rowing or I'll toss you all overboard!"

The threat came from a red-headed woman dressed in corset and bloomers, with a Colt .45 lashed to her waist. And as the crowded lifeboat marked *S.S. Titanic* lurched into the waves, she rowed too, rowed until her hands bled.

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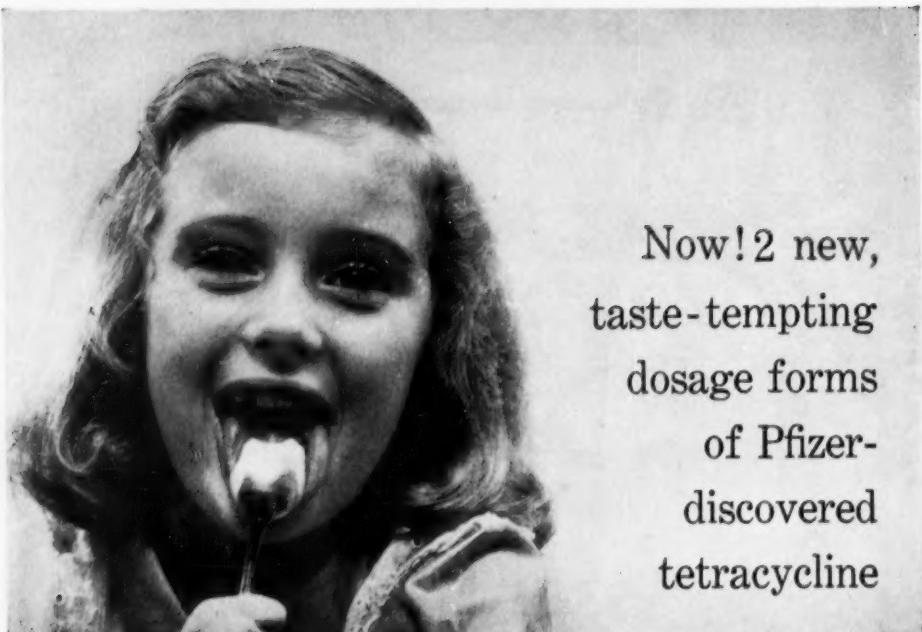


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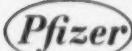
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**1. Cass & Wolf: Gastroenterology 20:149, 1952**

**2. Cantor: Am. J. Proctol. 3:204, 1952**

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- alcoholic beverages

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